The Journal of Pediatrics

VOL. 19 NOVEMBER, 1941 NO. 5

Original Communications

PRESIDENTIAL ADDRESS

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BOSTON, MASS.

IT BECOMES my duty and pleasure at this time to fulfill the provision of the By-Laws, which states that at the Annual Meeting "a presidential address shall be delivered." I have chosen as the subject of my address, "The American Academy of Pediatrics."

You have given me the opportunity during the last year to become familiar with the work of the Academy in a way that is difficult to appreciate if one's contacts have been confined, as mine had been previously, to service upon Regional or State Committees. The more general one's vision of the whole Academy program becomes, the greater is the realization of the breadth of its activities and the extent of its influence. I wish at this time to express to you my deep appreciation for the honor which you conferred upon me in electing me to serve as your President during the past year. It has been a great pleasure to become better acquainted with those of you whom I had known for a varying number of years and to make new friends throughout the membership. I cannot express too strongly my admiration for the work which you are doing nor speak too optimistically in relation to the possibilities of usefulness which lie ahead.

The Regional meetings were well attended this year and the programs excellent. The Reports of the Regional Chairmen have been placed in your hands. It was my good fortune to attend three of the Regional meetings, and Dr. Mitchell went to Region IV. Altogether 594 Fellows, over 42 per cent of the membership, registered. Including guests, the attendance was over 1500. By Regions, the registration was, Region I, 36 per cent of the members; Region II, 16 per cent; Region III, 58 per cent; Region IV, 66 per cent. The influence of the Academy is greatly enhanced by bringing together in each region such a large group to discuss the welfare of infants and children.

The Executive Board is the policy-making body of the Academy, and it tries to reflect the sentiment of the members. The actual work of the

Eleventh Annual Meeting of the American Academy of Pediatrics, Boston, October 9-11, 1941.

Academy is carried on by the various Committees. Since these Committees are so important in the life of the Academy, the Executive Board has given considerable thought this year to their functions and activities. The Committees have been classified into two main groups—Standing Committees and Special Committees—and the names of the Committees have been shortened whenever possible. The Standing Committees have been further divided into those with general activities and those with state activities. The Standing Committees are, broadly speaking, permanent committees. It is assumed that they will continue from year to year, although their concentrations of interest may vary somewhat from time to time. Standing Committees with general activities are those concerned with matters relating to the Academy as a whole. They study general problems and initiate broad activities under the direct supervision of the Executive Board. These Committees are:

COMMITTEE ON HONORARY FELLOWS
COMMITTEE ON PEDIATRIC AWARDS
COMMITTEE ON CENTRAL AND SOUTH AMERICAN SCHOLARSHIPS
COMMITTEE ON LEGISLATION
COMMITTEE ON MEDICAL EDUCATION
COMMITTEE ON HOSPITALS AND DISPENSARIES
COMMITTEE ON MENTAL HEALTH
COMMITTEE ON NURSING EDUCATION
COMMITTEE ON COOPERATION WITH THE AMERICAN MEDICAL ASSOCIATION
COUNCIL FOR PEDIATRIC RESEARCH
PROGRAM COMMITTEE
NOMINATING COMMITTEE

The Standing Committees with state activities are concerned with equally important problems but they function primarily through corresponding local committees in the various States. As contrasted with policy their function is work—work at the level of the local community—specific and practical. These Committees are:

COMMITTEE ON COOPERATION WITH GOVERNMENTAL AND MEDICAL AGENCIES
COMMITTEE ON COOPERATION WITH NON-MEDICAL GROUPS
COMMITTEE ON COOPERATION WITH THE AMERICAN LEGION
COMMITTEE ON THE FOETUS AND THE NEWBORN INFANT
COMMITTEE ON SCHOOL HEALTH
COMMITTEE ON CAMPS
COMMITTEE ON CONTACT INFECTIONS

Most of the Standing Committees have been very active this year. The full reports of their work have been placed in your hands. What they

have done and are doing is of vital importance to the children of this country. Through them the Academy influences directly or indirectly the welfare of every community. I should like to call your attention to a few of the matters discussed in the committee reports. The Chairmen of some of these Committees will speak to you later and you will be given an opportunity to ask them questions.

The Committee on Honorary Fellows is charged with the responsibility of recommending to the Executive Board the names of pediatricians in foreign countries who, by outstanding achievement, might properly become honorary members of the Academy. We have at the present time five such members. No new names have been added this year.

The Committee on Pediatric Awards has reported this afternoon through its Chairman. A great deal of time and effort is spent by the members of this Committee in reviewing the work of the many candidates for awards now offered by the Academy through the generosity of the Mead Johnson Company. That each year the awards have been so meritoriously decided is a tribute not only to their work but also to their discriminating judgment.

The Committee on Central and South American Scholarship has been successful in securing money sufficient to bring several physicians to this country for postgraduate study. Their energy in the pursuit of this endeavor has been another evidence of unselfish devotion to the interests of the Academy and through it to the improvement of pediatric practice. It has been a means of still further cementing the bonds of friendship between this country and our neighbors to the South. It is hoped that even more permanent and intimate associations may be established between all the pediatricians of the Western Hemisphere. Through the courtesy of Broadcasting Station WRUL, we have been able to send by short-wave a message to South America, in Spanish, during the course of this Annual Meeting.

The Committee on Legislation has kept careful watch over the Congress and has been active in protecting the children of America by favoring those Bills which have been desirable and opposing those which would affect them adversely. This Committee also prepares for your consideration proposed changes in the Constitution and By-Laws of the Academy.

The Committee on Medical Education performed an inestimable service in the early years of the Academy by its study of Pediatric Education. It is working continually through its three subcommittees to advance the quality of pediatric training and to increase the facilities, particularly in postgraduate instruction.

The Committee on Nursing Education is working closely with the National League of Nursing Education to improve the training of nurses in pediatrics.

The Committee on Mental Health is busy preparing a film which it is hoped may be ready for release during the coming year. This task has been under consideration for a long time. It is a difficult undertaking. We are confident that the project is in safe hands.

The Committee on Cooperation with the American Medical Association has kept us in contact with that National body of organized medicine and has sought to secure united action upon matters of mutual interest.

The Council for Pediatric Research explored a new field in its initial program of bringing together business firms with funds to be spent for research and medical groups with interest and skill to perform the work. The Council was originally an independent body functioning under the aegis of the Academy. It has now been reorganized as an Academy Committee and gives promise of being able to make a real contribution to the advancement of medical knowledge.

The Program and Nominating Committees speak by their deeds. I am sure that you will agree with me that their work has been well done. I should be guilty of gross negligence if I failed to call attention to the fact that the success of the scientific portion of this year's meeting is due in large measure to the untiring efforts of our Assistant Secretary, Dr. Edgar E. Martmer. He has labored long and faithfully to secure the leaders of the Round Tables and Panel Discussions. I should like to express to him your thanks as well as my own appreciation of what he has accomplished.

The Committee on Cooperation with Governmental and Medical Agencies, formerly called the Committee on Child Health Relations, has continued to advance the program, as outlined in the Chairman's report, of making "each State Fellowship of the Academy the principal advisory group for State Departments of Health and other official State agencies, and the State Medical Societies.

The Committee on Cooperation with Non-Medical Groups and Societies has prepared a brochure on the School Health Examination. This is designed to supplement the interest in this subject stimulated by the film, "When Bobby Goes to School," and to secure an examination for the school child of proper content and quality. "When Bobby Goes to School" continues to be received favorably throughout the country. There are eighty reels available and they are constantly in use. I wonder whether you appreciate the painstaking work and the many hours which went into the preparation of this film. There were many details which needed consideration. This Committee and the Executive Board have established certain policies in relation to the preparation and showing of films sponsored by the Academy which will govern and assist us in future similar enterprises.

The Committee on Cooperation with the American Legion has been especially helpful in relation to legislative measures. A most unde-

sirable Bill before Congress, which was discussed at our last meeting, was modified largely through the influence of this Committee and our Committee on Legislation.

The Committee on the Foetus and the Newborn Infant is at present working on standards for nurseries for newborn infants as part of a long-term program to reduce fetal and neonatal mortality.

The Committee on School Health has been stimulating, through the State Committees, active interest in school health service, which has met with an encouraging response.

The Committee on Camps has been active in many States in working to maintain and improve the medical supervision and health standards in camps.

The Committee on Contact Infections has been studying the best means of preventing the spread of tuberculosis to children through family and school contacts. There was a Round Table discussion at this meeting on the subject. We look for specific recommendations from this Committee in the near future.

The Special Committees are appointed to perform a limited task and when this task is accomplished, the committee is discharged. They may be asked by the Executive Board for recommendations in relation to matters which require study and consultation before wise action can be taken, or to carry out a specific project. They may be concerned either with policy or with general or local activities.

At the present time there are five such Committees:

COMMITTEE ON NATIONAL DEFENSE
COMMITTEE ON MOTHERS' MILK BUREAUS
COMMITTEE ON VITAMINS
COMMITTEE ON IMMUNIZATIONS AND THERAPEUTIC PROCEDURES FOR ACUTE INFECTIOUS DISEASES
COMMITTEE ON TUMOR REGISTRY

The Committee on National Defense has worked very hard since it was appointed. You heard last night about what it is doing. It is probable that this Committee will be even more active during the coming year and that many of you may be asked to assist in carrying on its program.

The Committee on Mothers' Milk Bureaus has been studying the question of standards and will report their recommendations at a later date.

The Committees on Vitamins and on Immunizations have each prepared brochures which you have received. These publications are valuable reference manuals and have met with widespread commendation and use. These Committees are being continued in order that revision of the publications may be made when and if new facts make such a procedure desirable.

The Committee on Tumor Registry: It has been suggested to the Executive Board that it would be desirable for the Academy to maintain a registry for tumors occurring in infancy and childhood. There are many questions which will need to be considered before such a plan is put into operation. The Committee will make recommendations as soon as a careful survey has been completed.

In addition to the Committees there are Liaison Representatives to various organizations with whom it is desirable for the Academy to be in contact. These Representatives report to the Executive Board when there are matters concerning which it should be informed or take action. The organizations with which we have this form of contact are:

NATIONAL MATERNAL AND CHILD HEALTH COUNCIL
MEDICAL ADVISORY COMMITTEE TO THE CHILD HYGIENE DIVISION OF THE CHILDREN'S BUREAU
NATIONAL CONFERENCE FOR COOPERATION IN SCHOOL HEALTH EDUCATION OF THE NATIONAL EDUCATION ASSOCIATION
NATIONAL FOUNDATION FOR INFANTILE PARALYSIS
AMERICAN CAMPING ASSOCIATION
PARENT-TEACHERS ASSOCIATION
AMERICAN PUBLIC HEALTH ASSOCIATION
REVISION OF THE UNITED STATES PHARMACOPEIA

The members of all the Committees and the Liaison Representatives are appointed by the President. It is one of his most important responsibilities. This year the Executive Board has adopted certain principles to guide the President in making these appointments:

1. No member of the Executive Board shall be chairman of any Committee nor serve on any Committee.
2. No Fellow of the Academy shall be a member of more than one Committee.
3. At least one member of a standing committee shall retire each year.

In the early days of the Academy it was inevitable that a relatively small number of men should hold a variety of positions. Now that the Academy has grown to its present proportions, it is desirable that as great a number as possible of the members shall be taking part in its activities. The application of these principles will help to accomplish this end.

In addition to the Committees of the Academy, which I have been discussing, there are also State Committees appointed by the State Chairmen. The State Chairmen are appointed by the President upon recommendation of the Regional Chairmen. The State Committees carry on

the work of the Academy Standing Committees with State activities, and they also perform many duties which deal with local problems within the state. At the request of the Executive Board, the Assistant Secretary has prepared a manual for State Chairmen which outlines the general work of the Academy and presents in some detail the duties of the State Chairmen and local Committees. It is hoped that this may prove of assistance to these officers in carrying on their work. It should be of especial value to new State Chairmen in acquainting them with their responsibilities.

I have spent considerable time in discussing the Committees because it is through them that the Academy functions. Existing agencies have been strengthened and official departments supported. New work has been initiated whenever it would benefit the health and welfare of children. You have accepted appointment upon committees often at considerable personal sacrifice. No Committee, nor any member of any Committee, has sought to receive personal credit for the work which has been done. This willingness to work unselfishly for the interests which the Academy represents has made the Academy a strong and influential body in this country today. It is universally known and respected as an association of professionally competent physicians from which disinterested advice may be obtained and which can be counted upon to accept and efficiently perform any task which it is called upon to undertake.

The American Board of Pediatrics is one of the important bodies which is raising the quality of pediatric practice in this country. This Board was organized through the joint action of the Academy, The American Pediatric Society, and the Pediatric Section of the American Medical Association. Three of the nine members of the Board are appointed by the Academy through the Executive Board. All of the members of the Board and all of the official examiners are members of the Academy.

THE JOURNAL OF PEDIATRICS has become one of the outstanding pediatric publications of this country and of the world. Its editorial board was originally appointed by the Academy and new members are added as necessary by your Executive Board. The wisdom shown in the selection of the first editorial board, and particularly in the choice of Drs. Veeder and McCulloch as Editors, is evidenced by the quality of the JOURNAL and its increasing circulation. We should be grateful to these men for their efficient and time-consuming work, and proud of their accomplishment.

The Executive Board has held two meetings this year; one in Chicago on May 31 and June 1, and one in Boston on Oct. 8. At these meetings consideration was given to a wide variety of subjects related to Academy activities. Reports were received from Regional Chairmen and Chair-

men of Committees. Many questions of policy were discussed. I should like to report briefly on some of the matters which are of general interest.

The finances of the Academy are in sound condition. Our invested funds do not yield as high a return as one would wish but safety of capital rather than rate of interest has guided the selection of investments. This, I believe, is a wise policy. Some of the Regions have been able to build up considerable reserve funds—largely through the exhibits at Regional meetings. It was voted by the Executive Board that all monies held by Regions should be accounted for each year and audited by certified auditors; that the funds should be deposited in the name of the Region of the Academy, and that at least two members of the Region should be empowered to sign checks. No suggestion of criticism of past actions was implied in this vote of the Executive Board, but it was felt that it was important to adopt business methods in dealing with all Academy funds. The procedure recommended to the Regions is the same as that employed by the office of the Treasurer of the Academy.

The Academy has maintained for some time a paid publicity service. This has served effectively in bringing to the attention of the country at large the ideals and activities of the Academy. This service has functioned largely through publicity in connection with the Annual and Regional meetings. The Committees have not received the benefit of this service as much as is desirable. It is hoped that in the future more use will be made of these available facilities in order that there may be widespread circulation of committee information and universal application of committee recommendations. The Chairmen of all the Committees are urged to communicate with the Secretary with regard to this matter.

The By-Laws of the Academy provide for the election by the Executive Board as Associate Fellows "persons, who, because of valuable service in any of the fields allied to pediatrics, are qualified to render assistance to the Academy in the accomplishment of its purposes." We have not taken sufficient advantage of this provision. There are many men and women who are working with children but who are not pediatricians. These persons could make a real contribution to the Academy because of their special knowledge in particular fields, and the Academy could be of service to them in many ways. The Executive Board welcomes nominations of Associate Fellows from any member of the Academy.

The Executive Board has voted to remit the dues of Fellows during active service connected with the present national emergency, if they so request. These Fellows will be kept on the mailing list but will not receive the JOURNAL.

A Resolution adopted by Regions III and IV was endorsed by the Executive Board and sent to the Surgeon-General of the Navy, the Surgeon-General of the Army, and to the Administrator's office of Coordinator of Health, Welfare and Related Defense Activities. This Resolution asked the respective officials to outline the objectives to be fulfilled in the defense program by pediatricians and called attention to the exceptional training of pediatricians in nutrition, contagious diseases, and child welfare. You have heard from the Committee on National Defense that this Resolution is being followed up by continuing efforts to secure the utilization of pediatricians in the fields of their special aptitudes.

At the suggestion of one of the Fellows, it was decided to include double listing of offices in the geographic section of the annual directory. This should be of benefit of those Fellows who maintain offices in more than one community. This seems to be a growing practice.

Arrangements have been made for the Secretary to publish a News Letter in the JOURNAL each month. By this means the members will be kept currently posted on Academy activities. It will serve as a means of mutual exchange of information between Regions and Committees. The Secretary will welcome communications which might be of interest in this connection.

The Executive Board has authorized during the last few years the publication of four Brochures, *The Health Record, Vitamins, Immunization Procedures, School Health Examination,* and two films, "When Bobby Goes to School," and one on "Mental Health" (in preparation).

You will see from this brief and inadequate review that the Academy covers a wide range of activities and influences the work for children in many communities. The growth of the Academy, in the short period of ten years, both in the number of members and in the importance of its program, is truly remarkable. It has not happened by chance. That its course has been so well directed, and its efforts so fruitful, is due in large measure to the wise guidance and indefatigable labors of our Secretary, Dr. Grulee. It has been a great pleasure to have worked with him during this last year. Without his constant assistance your President would have floundered and been lost in the midst of an impenetrable fog.

We have spoken almost entirely of what has been done but our eyes are fixed firmly upon the road before us. This is a changing world. The Academy must be ready to accept the challenge which new conditions will present. I have no hesitation in predicting great accomplishments in the future, greater even than those of the past. This is your organization. It will go forward as rapidly and as far as your vision sees and your energy directs. Every member has a part to play. Let us together resolve to continue in the great task of safeguarding and improving the health and happiness of the future citizens of this free country.

BACTERIOSTATIC AND BACTERICIDAL AGENTS OBTAINED FROM SAPROPHYTIC MICROORGANISMS

R. J. Dubos, Ph.D.
New York, N. Y.

THE field of studies which you have chosen to recognize by the E. Mead Johnson Award for 1941 is the outgrowth of observations dating from the very beginnings of bacteriology; the specific achievements which I shall discuss at some length today are the results of investigations carried out at the Hospital of The Rockefeller Institute, most of them in close collaboration with Dr. R. D. Hotchkiss. In thanking you for the honor bestowed upon me, therefore, I fully appreciate how much I owe to the past, and to the environment in which it has been my good fortune to work.

The phenomenon of antagonism between different species of microorganisms has been repeatedly observed; a recent review[32] lists 373 contributions which, directly or indirectly, deal with this topic, beginning with Pasteur's observation in 1877[27] that saprophytic bacteria may, under certain circumstances, decrease the infective power of the anthrax bacillus. Medical scientists were not slow in recognizing the potential value of microbial antagonism for the study of the problems of infection; in 1885 Cantani[2] expressed the hope that certain infections might in the future be treated with saprophytic organisms, antagonistic to the etiologic agents. Of the many examples of microbial antagonism which have been recognized, this discussion will consider only a very few, selected because fairly clear information is available concerning the mode of action of the antagonist.

Among bacterial contaminants which may inhibit the growth of other microbial species on nutrient agar plates, none is more common, or more obvious in its action, than *Pseudomonas pyocyanea*. Cultures of this organism have yielded soluble extracts which, under the name of pyocyanase, have been found to exert marked bacteriostatic and bactericidal effect against many unrelated microbial species.[12] In fact, around 1900, several reports appeared claiming the successful treatment with pyocyanase of a variety of infections. Although one may be skeptical concerning the significance of these clinical investigations, it remains true that pyocyanase exhibits a remarkable antibacterial activity in vitro. Indeed, it has been recently shown that one can isolate from old cultures of *Pseudomonas pyocyanea* three well-defined substances, (a) the pigment pyocyanine, (b) α-oxyphenazine, and (c) an oil called pyocyanic acid, all of which are endowed with antibacterial activity.[30] It appears also that pyocyanine is capable of inactivating the enzyme succinic de-

E. Mead Johnson Award, American Academy of Pediatrics, 1941. Presented at the Eleventh Annual Meeting, Boston, Mass., Oct. 10, 1941.

hydrogenase[21] a property which may explain its antibacterial effect. Unfortunately, the great toxicity of pyocyanine and pyocyanase for animal tissues may render them of little interest as chemotherapeutic agents.[21]

In 1929, Fleming observed that a strain of *Penicillum notatum*, growing as a contaminant on nutrient agar plates, inhibited the growth of pyogenic cocci.[13] The antagonistic activity of the fungus was traced to a soluble principle, penicillin, present in culture filtrates of the organism. The addition of penicillin to nutrient broth or agar was found to inhibit the growth of most gram-positive organisms, whereas gram-negative bacilli remained unaffected; use was made of this differential susceptibility for the preparation of a selective medium, containing penicillin, and which could be used in the isolation of *Hemophilus influenzae*. The recent work of the Oxford School of Pathology has revealed many interesting facts concerning penicillin.[1] The substance is readily soluble in organic solvents and can be separated by extracting the culture medium at pH 2.0 with ether or amyl acetate. Although the substance is readily inactivated at acid reactions, it is fairly stable in the form of the sodium or barium salt. The effect of penicillin is primarily bacteriostatic, rather than bactericidal and, as a rule, the gram-positive species are more susceptible to it than are the gram-negative bacilli; acid-fast bacilli are completely resistant. Nothing is known of its mode of action; it does not destroy the respiration of susceptible bacterial species (staphylococcus) but appears to prevent cellular division and give rise to giant forms.[14] Penicillin is not inhibited by serum, tissue extracts, and exudates; its toxicity appears to be low. In fact, it exhibits in vivo a striking therapeutic effect against experimental infections caused by pyogenic cocci; preliminary results obtained in human therapy have been very encouraging although the amounts of the substance available have not so far been sufficient to permit extensive clinical trials.

It is known that soil and sewage harbor an immense variety of microbial species, capable of performing almost any conceivable biochemical reaction, and of decomposing every type of organic substance. During the past few years, this point of view has found its application in the isolation from soil of new bacterial species selectively adapted to the study of several biochemical and immunologic problems.[4, 5] In particular, a systematic attempt was made to discover soil microorganisms that could attack the living cells of gram-positive cocci. To achieve this end, suspensions of living streptococci and staphylococci were added to a soil mixture, which was maintained at neutral reaction under aerobic conditions, in the hope that there would develop in the soil sample a microbial flora antagonistic to the gram-positive cocci. In fact, it was possible to isolate from this soil preparation a strain (BG) of *Bacillus brevis*—an aerobic sporulating organism—which produces a soluble principle extremely toxic to gram-positive bacteria. More recent studies have established that different strains of *Bacillus brevis* are

commonly distributed in nature and that most of them produce varying amounts of the same antibacterial agent.[3, 10, 25, 31] This agent is abundantly produced when *Bacillus brevis* is grown under aerobic conditions in peptone media; from these peptone cultures it is possible by different treatments to release in solution several active fractions which differ, not only in chemical composition, but also in antibacterial and other biologic properties. These different fractions all appear to be breakdown products of a common mother substance, present in the bacterial cell, and to result from the manipulations inherent to the techniques of extraction and purification.

Acidification of the autolyzed culture of *Bacillus brevis* gives a precipitate from which the antibacterial substance can be obtained in solution by extracting with neutral buffer.[3] This water soluble material is protein in nature; on treatment with acid alcohol or acetone, it yields an inactive precipitate (a protein) and an active fraction which is soluble in these organic solvents, but insoluble in aqueous media.[8]

This same alcohol soluble, water insoluble fraction, which has been called tyrothricin, can be more conveniently obtained by precipitating the whole autolyzed culture of *Bacillus brevis* with HCl at pH 4.7, extracting the precipitate with 95 per cent alcohol, separating the active alcohol soluble fraction by filtration or centrifugation, and precipitating from it the active material by diluting with 10 volumes of 1 per cent NaCl. As stated above, this tyrothricin fraction cannot again be brought into true solution in aqueous buffer, although it can be dispersed as a stable colloid solution in the absence of electrolytes; glucose and glycerine do not precipitate the system and can be used therefore for the preparation of isotonic colloidal solutions. Addition of bile or many other detergents greatly enhances the stability of the product. Tyrothricin is believed to be a product of some form of alteration or degradation of the soluble protein material mentioned above.[10]

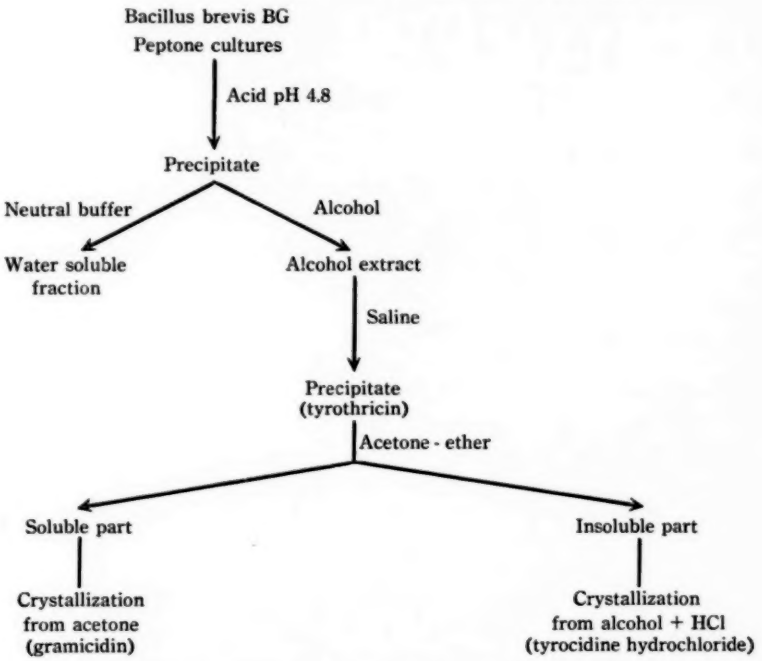
Both the water soluble protein fraction and the alcohol soluble, water insoluble tyrothricin fraction exhibit antibacterial activity in vitro and in vivo. Because of the greater ease of preparation, tyrothricin has been much more extensively studied. It has now been found that tyrothricin is a mixture of at least two active substances which have been crystallized and called gramicidin and tyrocidine. The chemical and biologic properties of the mixture, tyrothricin, appear to be adequately explained in terms of its component parts. It appears preferable, therefore, to limit our discussion to the properties of the pure substances gramicidin and tyrocidine, although many workers have used the more readily available tyrothricin, especially for in vivo studies.

Gramicidin and tyrocidine can be separated and crystallized by making use of their differential solubilities in acetone and ether, and in particular of the fact that the salt, tyrocidine chloride, is considerably less soluble than the neutral gramicidin in mixtures containing ether.[20] Gramicidin is a polypeptide which contains no free amino or carboxyl

group. Analytic data appear compatible with a molecular weight of 1054 or 1413. It crystallizes in the form of colorless platelets with pointed ends.[19, 20] Tyrocidine is also a polypeptide, but containing free basic amino groups. Analytic data indicate a probable molecular weight of 2500. It crystallizes as fine colorless needles or rods.[19, 20] In both polypeptides a large percentage of the α amino acids have the d- configuration so rarely found in natural products.[22]

TABLE I

PREPARATION OF TYROTHRICIN, GRAMICIDIN, AND TYROCIDINE



In spite of their common origin, and of the fact that both substances are polypeptides, and both behave as surface active substances,[16] gramicidin and tyrocidine differ not only in other chemical properties, but also in biologic activity. Tyrocidine, when tested in buffer solutions, in the absence of serum, tissue extracts or peptones, affects both gram-positive and gram-negative microbial species. Gramicidin, on the contrary, is completely inactive against gram-negative bacilli, moderately active against meningococci and gonococci, and highly inhibitory to practically all the gram-positive species so far tested (with the exception of acid-fast bacilli).[10] Mention must also be made at this time that it is possible to isolate from susceptible bacterial species, variant forms which are more resistant to gramicidin and which remain resistant even

after repeated subcultures in media free of the substance; these resistant forms are readily obtained from staphylococcus cultures, much less so from group A streptococci.[9]

Gramicidin never causes the lysis even of the most susceptible organisms. Tyrocidine, on the contrary, lyses many bacterial species; there is good evidence, however, that this lytic effect is not a direct one, but only a secondary autolytic process which follows upon the death of the cell and which occurs only in species endowed with active autolytic enzymes (pneumococcus and staphylococcus for instance).[10]

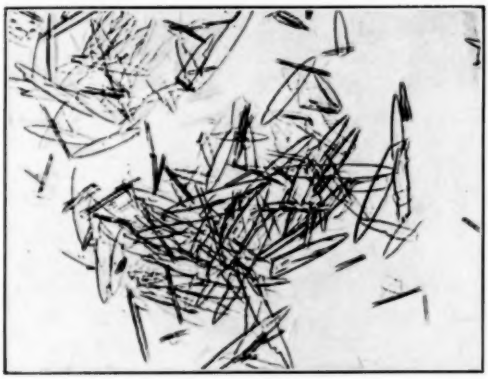


Fig. 1.—Photomicrograph of crystals of gramicidin. ×225. (Courtesy of Dr. R. D. Hotchkiss.)

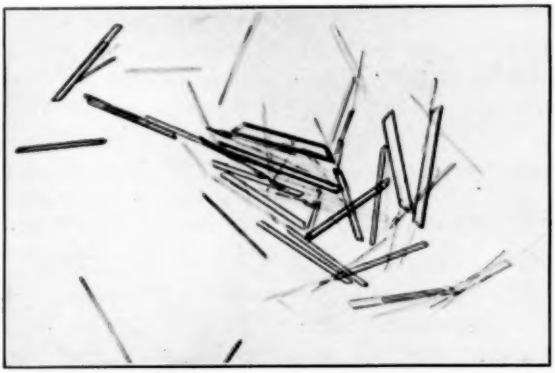


Fig. 2.—Photomicrograph of crystals of tyrocidine hydrochloride. ×320. (Courtesy of Dr. R. D. Hotchkiss.)

The effect of gramicidin is inhibited only to a small extent by serum, tissue extracts, or peptones; of all substances tested, the phospholipid phosphatidyl-serine is the only one which has been found to be very inhibitory.[9] Many tissue constituents, on the other hand, inhibit the activity of tyrocidine, and it is difficult to detect the effect of this substance on gram-negative bacilli in peptone solutions.[10]

Tyrocidine immediately destroys the metabolic activity not only of bacterial, but also of animal cells, as recognized by loss of oxygen uptake, of reducing ability and of acid production. On the contrary, these essential metabolic functions are unimpaired by gramicidin—even in the case of the most susceptible cells—under a variety of experimental conditions.[11]

TABLE II

COMPOSITION OF GRAMICIDIN

Molecular weight in camphor, approximately 1350
Molecular weight by tryptophane content, 530, 1050, 1600
Neutral polypeptide: No $-NH_2$ or $-COOH$ groups
Water insoluble
Contains tryptophane
Contains leucine
Contains alanine
Contains amino hydroxy compound (serine, isoserine, etc.)
Contains no $-CONH_2$, tyrosine, or basic amino acids
Contains no methoxyl, acetyl, or higher fatty acid

TABLE III

COMPOSITION OF TYROCIDINE

Approximate formula, $C_{66}H_{92}N_{13}O_{13}$ HCl
Salt of basic polypeptide
Contains free amino group ($-NH_2$)
Contains two amide groups ($-CONH_2$)
Contains aspartic acid
Contains tyrosine
Contains tryptophane

It appears, therefore, that tyrocidine behaves like a general protoplasmic poison, whereas the effect of gramicidin is of a much more subtle nature. This is illustrated by the fact that in the case of some bacterial species at least, the effect of gramicidin is bacteriostatic and not bactericidal. Cells of group D streptococci, for instance, can be maintained for weeks in the presence of an excess of gramicidin without losing their viability; the addition of 0.001 mg. of the substance to 5 c.c. of medium, however, is sufficient to inhibit the growth of these organisms.[9]

Tyrocidine loses most of its antibacterial activity in the presence of animal tissues. Gramicidin, on the contrary, when applied locally at the site of the infected area, does protect experimental animals against infection with susceptible pathogenic agents. For instance, 0.001 mg. of the substance injected intraperitoneally is sufficient to protect mice against 10,000 fatal doses of pneumococci or group A streptococci. It must be stated at this time, however, that gramicidin is almost completely inactive against systemic infections even when injected intravenously. This ineffectiveness may be due to physical properties (lack of solubility) which prevent diffusibility of the agent throughout the tissues, or to the inhibitory effect upon its activity of certain tissue components (phosphatidyl-serine for instance) or perhaps to the toxic reactions which follow the intravenous injection of the substance.

The fact that gramicidin is effective in vivo when tested under appropriate conditions, and that some attempts have been made to use it in therapy, gives special interest to a knowledge of its effect on the cells of animal tissues. Gramicidin does not seem to affect the growth and behavior of animal cells in tissue culture,[17] nor does it alter the oxygen uptake of polymorphonuclear leucocytes resuspended in buffer solutions.[9] Bull spermatozoa, on the other hand, are extremely susceptible to it as evidenced by loss of motility and modification of the metabolism.[18] Both gramicidin and tyrocidine are hemolytic; the hemolysis by gramicidin, however, though caused by much smaller amount, is slow and entirely prevented in vitro by the presence of low concentrations of glucose and mannitol.[10, 15] Both compounds are highly toxic to dogs and mice when injected into the blood stream.[26] It is possible that the hemolytic action of gramicidin may contribute to its toxicity in the blood stream.[17] On the other hand, gramicidin, either in the purified form or mixed with tyrocidine in tyrothricin, appears to exhibit less toxicity when applied locally, for instance on mucous membranes, wounds or when injected by subcutaneous, intramuscular, or intrapleural routes.[17, 28, 29]

On the basis of this knowledge some attempts have already been made to use gramicidin (especially in mixture with tyrocidine as tyrothricin) for the local treatment of localized infections. The substance has been tested in emulsion in distilled water, dilute glycerine solutions, or mixed with oil in a number of conditions associated with gram-positive pathogenic agents—bovine mastitis (caused by group B streptococci),[23, 24] empyemas,[28] sinusitis,[17] stasis ulcers,[17] etc. In a few preliminary observations, tyrothricin has also been used in an attempt to eliminate hemolytic streptococci from the rhinopharynx of carriers.[29]

It is obvious that the amount of information available is too scanty to warrant an opinion concerning the potential value of penicillin and gramicidin as chemotherapeutic agents. It appears justified to hope, however, that these substances may be of some interest to the student of infectious diseases, even if they fail to find a place in therapy. Both penicillin and gramicidin, and perhaps other antibacterial substances obtained from saprophytic microorganisms[33] have revealed new types of organic compounds endowed with remarkable bacteriostatic and bactericidal activity. An exact knowledge of the chemical structure of these new compounds, and especially of the molecular groups to which they owe their biologic activity, will give to the chemist valuable clues for the synthesis of new substances which, one may hope, will be of greater practical value than the naturally occurring substances.

The mechanism of the bacteriostatic and bactericidal effects exerted by these new substances also presents problems of great theoretical and practical interest. It is worth noting, for instance, that the gram-positive species on the one hand, and the gram-negative bacilli on the other, exhibit a striking difference in their susceptibility to many anti-

bacterial agents, a fact which must depend on some fundamental difference in cellular structure between the two groups of organisms.[6] It is also remarkable that sulfanilamide, penicillin, and gramicidin can be clearly set apart from the classical antiseptics which are general protoplasmic poisons. All three substances are primarily bacteriostatic rather than bactericidal in their action. Since they do not destroy the respiration of bacteria, one may assume that the inhibition of growth which they cause depends not upon interruption of the cellular metabolism as a whole, but rather upon some subtle interference with certain individual reactions.[7] To interrupt the pathogenic career of an infectious agent, therefore, it is not necessary to kill the invading cell, but only to block one step in its metabolic path by some specific inhibitor.

The discovery of new bacteriostatic and bactericidal agents produced by saprophytic microorganisms is not an end in itself. But rather it gives us new tools for the study of those cellular structures and those metabolic systems of infectious agents which are essential to pathogenicity and which are vulnerable to attack by specific agents.

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CONSTITUTIONAL BARRIERS TO INVOLVEMENT OF THE NERVOUS SYSTEM BY CERTAIN VIRUSES, WITH SPECIAL REFERENCE TO THE ROLE OF NUTRITION

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THE studies which I propose to review in this communication were prompted by the desire to discover and to understand the mechanisms underlying the varying responses of different individuals to infections with viruses which affect the nervous system. If we consider a very typical virus disease of the nervous system such as poliomyelitis, we are impressed with the fact that only a small proportion of the individuals who become infected with the virus develops the serious paralytic form of the disease while the great majority escapes with nonparalytic, abortive, or completely inapparent attacks. This difference in behavior of the infected host is also evident to a greater or lesser degree in a variety of other virus infections of the nervous system. The explanation which for years has soothed our inquiring spirit and curiosity stated that the repeated exposure to small subinfective doses of these viruses gives rise to an immunity which permits the host to resist subsequent infection with larger doses. While there is no good evidence that such subinfective doses (which may be defined as amounts of virus too small to undergo multiplication) can give rise to such immunity, it has become increasingly evident in recent years that the situation may actually perhaps be the other way around; namely, that the reason many individuals exhibit evidence of immunity without a history of having experienced apparent disease is that upon first exposure to an infective dose their tissues were so constituted as to permit successful arrest of viral multiplication or dissemination.

The present studies began when during the course of work with Drs. P. K. Olitsky and H. R. Cox on the virus of vesicular stomatitis of horses, it was observed that whereas young and old mice were equally susceptible to the smallest amounts of virus injected directly into the brain, there was a marked difference in the behavior of the young and old animals when the virus was introduced in some peripheral site, such as the nose, eye, peritoneal cavity, muscle, or skin. The young regularly developed ascending paralysis or encephalitis, while the old were resistant to a varying degree, depending upon their age and route of inoculation. The development of this resistance was shown to be dependent neither on prior exposure to the virus nor on the presence of antibodies in the blood and appeared at different ages for different routes of inoculation. Thus, after injection into the peritoneal cavity the virus

Presented at the eleventh annual meeting of the American Academy of Pediatrics, Boston, October 10, 1941, E. Mead Johnson Award.

From The Children's Hospital Research Foundation and Department of Pediatrics, University of Cincinnati College of Medicine.

no longer produced any apparent disease in mice as young as 15 days, while after intramuscular inoculation mice of this age regularly developed a fatal ascending paralysis and the first evidence of resistance did not appear until the fourth week of life. Mice older than 5 or 6 weeks were practically 100 per cent resistant to intramuscular injection of as much as ten million times the amount of virus which would have sufficed to kill them if it were introduced directly into the brain. Some mice resist virus inoculated into the vitreous of the eye as early as the third week of life, while more than 90 per cent are resistant after the fourth and fifth weeks. When the virus is instilled intranasally, only a few mice are resistant between the fourth and seventh weeks of life, while after the second and third months, depending upon the amount of virus administered, 50 to 90 per cent remain well. That this resistance which develops with increasing age is chiefly a matter of a change in relationship between specific tissues and a specific virus was further suggested by the observation that there was little difference between young and old mice when the equine encephalomyelitis virus was given intranasally; after intramuscular or intraperitoneal inoculation, however, older animals become resistant, although at different ages for the eastern and western types of the virus.

It was clear that in order to understand the nature of the changed host-virus relationships with increasing age, it was necessary to know in great detail the natural history of infection following the introduction of each virus by different routes. And so by extensive histologic studies and numerous subinoculation tests, the pathways of virus were mapped by different routes in young, susceptible animals following inoculation and compared with the course of events obtaining in the resistant ones. The results emerging from these investigations revealed many distinct patterns and pathways of virus progression and dissemination which varied not only with the route of inoculation, but also with the species of the host and type of virus. Incidentally, these results also shed light on the nature of the arrested infection in the resistant animals. It became apparent that the chief difference in the course of events following intracerebral and peripheral inoculations of vesicular stomatitis virus resulted from the fact that after introduction directly into the brain, the virus entered the ventricular system and thus could spread throughout the central nervous system along an "open" pathway, while after peripheral inoculation, the evidence pointed to progression along a "closed" system of neurons and their processes, not only from the periphery to the brain, but also along specific tracts within it. It was thus clear that as long as the virus could spread indiscriminately along an open system, fatal encephalitis resulted. Similarly it emerged that after peripheral inoculation into the resistant animals, the progression of the virus was halted at different sites, depending upon the pathways which it had to pursue.

The types of so-called barriers which were encountered are summarized in Table I. It may be seen that progression of vesicular stomatitis virus could be arrested at the retina when the virus was introduced into the vitreous of the eye, at the muscle or myoneural junction when it was injected in the muscle, and at the anterior olfactory region within the central nervous system, when it was instilled intranasally in old resistant mice. It is interesting to note that guinea pigs which are quite mature and in a certain sense self-sufficient at birth exhibit a resistance to neuroinvasiveness of this virus at the end of the first week of life (younger animals have not been tested) which is acquired by mice at a considerably later age. Even so the progression of nasally instilled virus is halted in different sites in the young and old guinea pigs; in the young, the barrier is within the central nervous system between the rhinencephalic cortex or diencephalon and the remainder of the brain, while in the old it is generally between the nasal mucosa and the olfactory bulbs. The course of infection with the viruses of eastern and western equine encephalitis in mice and guinea pigs was found to be different from that of vesicular stomatitis in that after introduction by certain routes these viruses must grow through or otherwise traverse certain blood vessels before the nervous system can become affected. Rather distinct patterns of resistance with increasing age were also found to obtain in the case of these viruses, and a study of the resistant animals revealed that they could experience a clinically inapparent systemic infection without involvement of the nervous system because the virus either did not multiply as well in the blood vessels or failed to traverse them for some other reason. It may be interesting to recall here that in the first human epidemic of eastern equine encephalitis 70 per cent of the cases were in children under 10 years of age.

During the course of these studies the question naturally arose as to what mechanism was responsible for the arrest of virus progression or dissemination at the particular sites listed in Table I. The possibility that these apparent barriers were not pre-existent but came into being during the course of infection as a result of a rapidly developing generalized immunity was the first to be considered and investigated. All the evidence that could be accumulated, however, indicated that the conditions which determined the difference between susceptibility and resistance came into play at the very beginning, or, at any rate, long before any specific immune response, regardless how short its latent period, could begin to exert its effect. It was shown, furthermore, that at a time when a considerable amount of virus had spread from the nose to the anterior rhinencephalon and failed to progress further in resistant mice, it was possible to produce a fatal encephalitis in these animals by an intracerebral injection of a minimal amount of virus, thus indicating that at the time the progression of virus was arrested the remainder of the brain was still susceptible. It was also found that vesicular stomatitis

virus could multiply in the muscle of the young susceptible mice but not in the old resistant ones. That the real barrier was thus in the muscle or myoneural junction from the beginning became even more evident following the demonstration that when this barrier was circumvented by direct intraneural injection of the virus, the old mice developed a fatal ascending myelitis. The fact that the appearance of resistance could vary from two weeks to two months of age, depending upon the virus and the tissue over which it had to pass or multiply, and the fact that for a given virus, route of inoculation, and host the spread was practically always arrested at the same site, were additional points in favor of definite pre-existing barriers rather than rapidly acquired generalized immunity. The evidence that newborn animals develop immunity more slowly and poorly in response to a variety of antigens has no bearing on this problem, not only because of the factors just mentioned, but especially in view of Morgan's recent studies which indicate that the capacity for an appreciable immune response to eastern equine encephalomyelitis virus is already present at an age when the majority of animals are still susceptible. With regard to the nature of these pre-existing barriers, the available data suggest that they may represent tissues in which the virus can either multiply not at all or not enough to be able to advance to the next zone which contains the fully susceptible tissue, involvement of which is necessary to give rise to clinical signs of infection. In other words, not all tissues in the same animal are necessarily equally susceptible to a given virus, and when the virus must travel along distinct cellular and neuronal pathways, such insusceptible zones can form a barrier to its further progression.

I need hardly stress that the mechanism of resistance to viral neuroinvasiveness which I have just described is only one among a number of others which may operate to determine the type of disease produced by neurotropic viruses. It is, however, a mechanism that appears to be closely linked to other phenomena of growth and development and as such especially lends itself to experimental investigation and perhaps modification. For a study of a number of factors which may prevent or enhance the development of this "maturation resistance," we selected the response to intramuscular injection of vesicular stomatitis virus in mice because a change from 100 per cent susceptibility (i.e., development of ascending paralysis) to practically 100 per cent resistance (i.e., failure to exhibit any signs of disease) takes place between the fourteenth and thirty-fifth days of life. This work, carried out in collaboration with Dr. Carl E. Duffy, included an investigation of the role of certain hormones and of nutrition on the development of this "maturation resistance" and can be touched upon only briefly in this communication. Because the development of this particular type of resistance coincides with the appearance of sexual maturity in the mice, an attempt was made to determine whether animals with an induced precocious sexual maturity would also become resistant at a corre-

TABLE I

LOCALIZED BARRIERS AS FACTORS IN PREVENTING OR ARRESTING INVOLVEMENT OF THE NERVOUS SYSTEM BY CERTAIN VIRUSES

VIRUS	HOST	ROUTE OF INOCULATION	SUSCEPTIBILITY OF YOUNG AND OLD	PROBABLE SITE OF BARRIER IN RESISTANT ANIMALS
Vesicular Stomatitis	Mouse	Intracerebral	Equally susceptible	None
		Intraocular	Young, encephalitis regularly Old, more than 90 per cent resistant	Retina
		Intramuscular Subcutaneous (pad)	Young, ascending myelitis Old, 100 per cent resistant	Muscle or myoneural junction Epithelium or nerve endings
		Intranasal	Young, encephalitis regularly Old, resistance varies from 50 to 90 per cent	In central nervous system, anterior olfactory region
	Guinea pig	Intracerebral	Young guinea pigs and mice equally susceptible; old guinea pigs slightly less	None
		Intramuscular Intra- and subcutaneous (pad)	Young and old resistant	Myoneural junction and specialized nerve endings
		Intranasal	Young, occasionally encephalitis Old, 100 per cent resistant	Young, (a) Between olfactory cortex and remainder of brain; and (b) between diencephalon and remainder of brain Old, generally between nasal mucosa and olfactory bulbs

Eastern Equine Encephalitis	Mouse	Intracerebral	Equally susceptible	None
		Intranasal	Equally susceptible	None
		Intramuscular	Young, 95 per cent encephalitis, 5 per cent ascending myelitis Old, 95 per cent resistant beyond 3 months of age	Blood vessels (generally)
Western Equine Encephalitis	Mouse	Intracerebral	Equally susceptible	None
		Intranasal	Old and young susceptible Old resistant to smaller doses	?
		Intramuscular	Young: 15 days, majority encephalitis; few ascending myelitis; 21 days, 60 per cent ascending myelitis; 20 per cent encephalitis; 20 per cent resistant	Blood vessels
			30 days and older, 90 to 100 per cent resistant	Muscle or myoneural junction
St. Louis Encephalitis*	Mouse	Intracerebral	Equally susceptible	None
		Intranasal	Equally susceptible	None
		Intramuscular	Young, some encephalitis; others ascending myelitis Old, resistant (with few exceptions)	Not determined

*Unpublished observations made in collaboration with Dr. Robert Ward.

spondingly earlier age. Gonadotropic hormone (gonadogen) injected daily beginning on the fifth day of life brought about enlargement and descent of testes in males and opening of the vagina and marked enlargement of the uterus and ovaries in the females within about twelve days. However, despite the presence of these distinct signs of sexual development, almost two weeks earlier than normal, these animals tested at 21 days of age were just as susceptible to the virus as their untreated litter mates. Preliminary experiments with the pituitary growth hormone, antuitrin G, and with desoxycosticosterone (because of its presumable effect on cell permeability) also yielded no significant results. However, carefully controlled studies on mice bred in our own laboratory have revealed that nutrition during the period of early growth can play a distinct role in the development of this type of "maturation resistance."

The nutrition of the growing mice was experimentally conditioned in two distinct ways: one, by modifying the maternal diet during the nursing period (which in mice includes most of the first four weeks of life) and two, by weaning the animals prematurely at 2 weeks of age (i.e., when they are still 100 per cent susceptible) and raising them on various selected diets. In the first group the mothers remained on a "full natural" diet consisting of a powder prepared from a variety of whole grains, tankage, meat scraps, dried milk, salts supplemented with whole milk, yeast, and cod-liver oil for two days after delivery, at which time they were changed to the various diets indicated in the chart; the offspring were left with their mothers for four weeks and then continued on the respective diets. The resistance of the various groups of mice was tested at the indicated ages by an intramuscular injection of approximately ten million minimal cerebral lethal doses, an amount of virus which regularly produced a fatal ascending paralysis in all mice inoculated at 2 weeks of age. It may be seen in Chart I that among the offspring whose mothers were continued on the "full natural" diet, 83 per cent were resistant at 4 weeks and 97 per cent at 5 weeks of age; still older mice have almost invariably all been resistant. In order to be able to study the effect of specific dietary factors it was necessary to obtain a base line with a simpler purified diet from which various substances could be withdrawn one at a time. This purified diet consisted of vitamin-free casein, corn starch, lard, and salt mixture supplemented with cod-liver oil, yeast, and wheat germ oil. On this simple vitamin supplemented diet the resistance of the offspring, although somewhat slower in development in some individuals, reached 97 per cent by the sixth week of life. When the yeast in this diet was autoclaved sufficiently to eliminate the heat-labile B complex, only 14 out of about 100 offspring lived long enough to be tested at 4 weeks of age and none of them was resistant. When thiamin in amounts of 0.5 mg. per 100 Gm. of diet (or 1:200,000) was added, the offspring continued to nurse and survived, but resistance developed more slowly than in the controls al-

though it reached 87 per cent by 6 weeks of age. It remains to be determined whether larger quantities of thiamin will suffice to eliminate this lag or whether another factor in the heat-labile B complex in addition to thiamin is required during the first weeks of life. A remarkable effect on growth and resistance was also obtained when rice polishings concentrate was substituted for yeast. The mice survived but grew poorly, and only 4 per cent were resistant at 4 weeks, 7 per

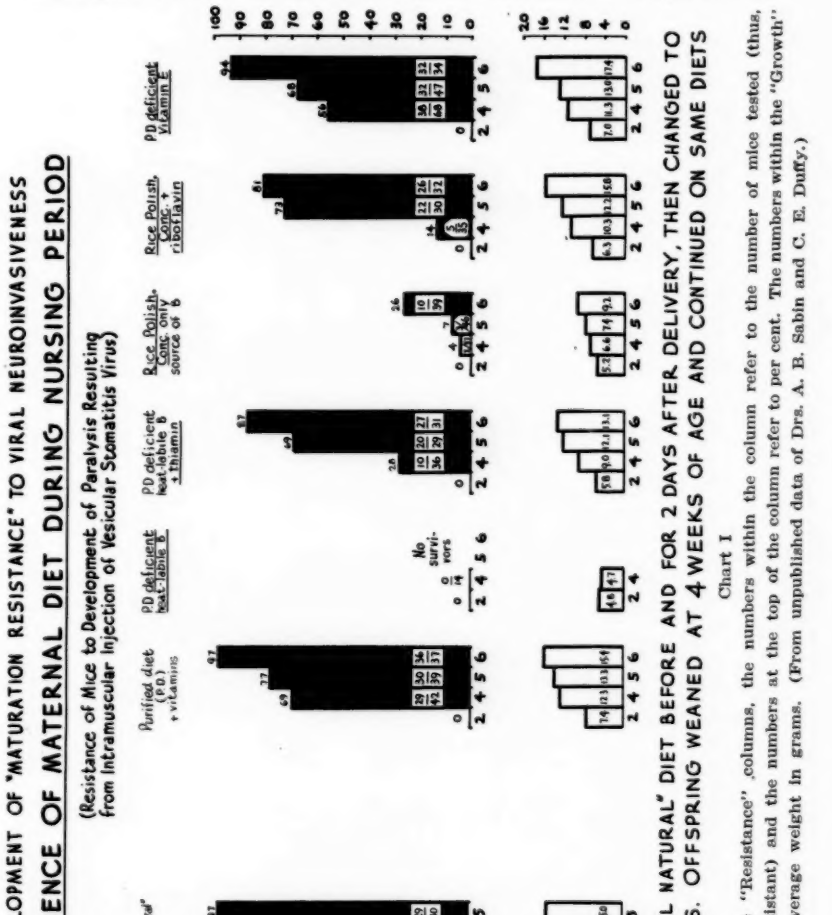
DEVELOPMENT OF "MATURATION RESISTANCE" TO VIRAL NEUROINVASIVENESS
INFLUENCE OF MATERNAL DIET DURING NURSING PERIOD
(Resistance of Mice to Development of Paralysis Resulting from Intramuscular Injection of Vesicular Stomatitis Virus)
"Full natural" diet
Purified diet (PD) + vitamins
PD deficient heat-labile B
PD deficient heat-labile B + thiamin
Rice Polish. Conc. only source of B
Rice Polish. Conc. + riboflavin
PD deficient vitamin E
Percent
RESISTANCE
Number of mice well & without paralysis
Age in weeks
Gms
GROWTH
Age in weeks
MOTHERS ON "FULL NATURAL" DIET BEFORE AND FOR 2 DAYS AFTER DELIVERY, THEN CHANGED TO INDICATED DIETS. OFFSPRING WEANED AT 4 WEEKS OF AGE AND CONTINUED ON SAME DIETS

Chart I

Charts I-IV.—In the "Resistance" columns, the numbers within the column refer to the number of mice tested (thus, $\frac{62}{75}$ = 62 of 75 mice resistant) and the numbers at the top of the column refer to per cent. The numbers within the "Growth" columns refer to the average weight in grams. (From unpublished data of Drs. A. B. Sabin and C. E. Duffy.)

cent at 5 weeks, and 26 per cent at 6 weeks of age. When crystalline riboflavin (0.7 mg. per 100 Gm. of diet) was added, both growth and resistance increased, although a certain lag was again encountered with

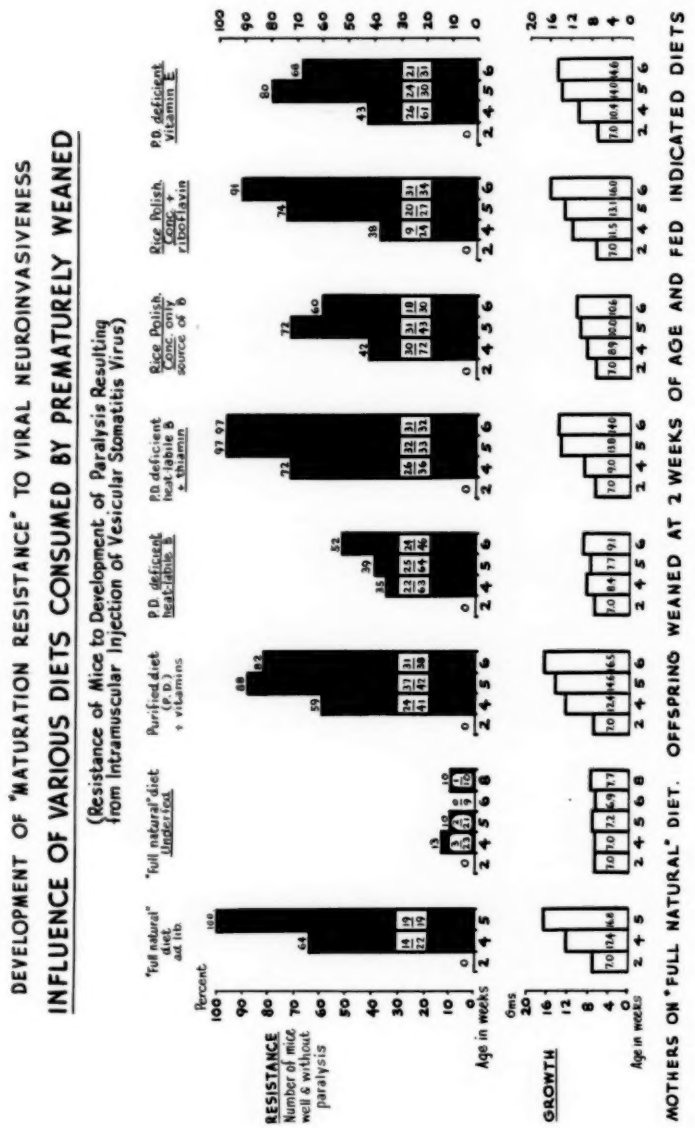
DEVELOPMENT OF "MATURATION RESISTANCE" TO VIRAL NEUROINVASIVENESS
INFLUENCE OF VARIOUS DIETS CONSUMED BY PREMATURELY WEANED
(Resistance of Mice to Development of Paralysis Resulting from Intramuscular Injection of Vesicular Stomatitis Virus)
"Full natural" diet ad lib.
"Full natural" diet Undefined
Purified diet + P.D. + vitamins
P.D. deficient heat-labile B
P.D. deficient heat-labile B + Vitamin
Rice Polish. Conc. only source of B
Rice Polish. Conc. + riboflavin
P.D. deficient vitamin E
RESISTANCE Number of mice well & without paralysis
Percent
Age in weeks
GROWTH
Gms
MOTHERS ON "FULL NATURAL" DIET. OFFSPRING WEANED AT 2 WEEKS OF AGE AND FED INDICATED DIETS

Chart II

only 14 per cent resistant at 4 weeks of age. Here also it remains to be determined whether larger quantities of riboflavin or some additional factor of the B complex not contained in rice polishings will be re-

quired to accelerate the development of this "maturation resistance." Vitamin E deficiency (i.e., removal of wheat germ oil from the diet) did not appear to exert a significant effect.

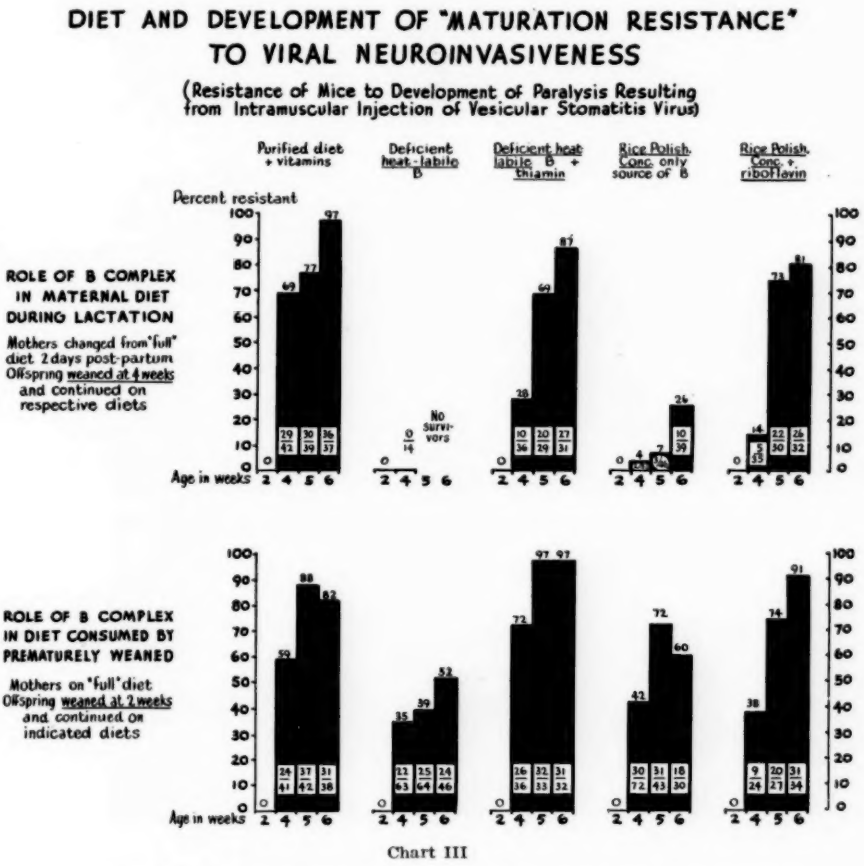
DIET AND DEVELOPMENT OF "MATURATION RESISTANCE" TO VIRAL NEUROINVASIVENESS
(Resistance of Mice to Development of Paralysis Resulting from Intramuscular Injection of Vesicular Stomatitis Virus)
Purified diet + vitamins
Deficient heat-labile B
Deficient heat-labile B + thiamin
Rice Polish. Conc. only source of B
Rice Polish. Conc. + riboflavin
Percent resistant
ROLE OF B COMPLEX IN MATERNAL DIET DURING LACTATION
Mothers changed from "full" diet 2 days post-partum
Offspring weaned at 4 weeks and continued on respective diets
No survivors
Age in weeks
ROLE OF B COMPLEX IN DIET CONSUMED BY PREMATURELY WEANED
Mothers on "full" diet
Offspring weaned at 2 weeks and continued on indicated diets

Chart III

Chart II shows the effect of the same diets on mice with a fourteen days' head start of nursing on properly nourished mothers, as well as the role of premature weaning and the influence of a quantitatively inadequate diet. On the "full natural" diet not as many of the prematurely weaned mice were resistant at 4 weeks of age (many mice lost weight for several days after weaning) but 100 per cent were found to be resistant at 5 weeks. When this full diet, especially rich in vitamins, was fed only in sufficient amounts to maintain the weight at the time of weaning, most of the mice survived and increased in size but approximately 90 per cent failed to acquire this special type of resistance even so late as the eighth week of life. Fairly good resistance developed on the purified, vitamin supplemented diet. However, a marked inhibition

in development of resistance resulted when the heat-labile B complex was eliminated, and addition of thiamin (0.5 mg. per 100 Gm. diet) to this deficient diet produced excellent results, which in this instance

Chart IV

were fully apparent at 4 weeks of age. An appreciable diminution in the number of 4-week-old mice with acquired resistance occurred with the diet containing rice polishings concentrate as the only source of B complex, and the addition of riboflavin, although without effect at this age, seemed to be beneficial later on. An irregular retarding effect of vitamin E deficiency also seems to be present in this group.

When one compares the effects exerted by the vitamin B complex in the two groups of animals (Chart III), it is interesting to note that the prematurely weaned mice, which, however, have had two weeks of nursing on properly nourished mothers, are influenced to a much lesser degree by subsequent deficiencies than are the offspring whose mothers are themselves on these deficient diets during the first two weeks after delivery. While optimum nutrition during the first two weeks of life is thus especially important, it is nevertheless clear that unimpeded growth during the next two or three weeks is essential to the development of this resistance. More marked in its inhibiting effect than any of the vitamin deficient diets tested during this period of rapid growth was the quantitatively inadequate vitamin-rich diet which failed to supply sufficient protein, carbohydrate, and fat. These underfed mice increased in size (Chart IV) and matured in other respects, but the changes in the muscles or myoneural junctions which develop with increasing age and are the basis of the resistance in the well-nourished animals obviously failed to appear. It is interesting to note, however, that the same dietary deficiencies which could prevent or retard the appearance of this resistance have thus far failed to break it down once it has become thoroughly established in full-grown animals.

In conclusion I should like to stress the following points:

1. That the relative insusceptibility or inavailability of certain specific tissues rather than resistance or immunity of the whole animal may function as a barrier to the progression of certain neurotropic viruses and thus prevent the development of clinically apparent disease of the nervous system;

2. That for some viruses and for some tissues and species this relative insusceptibility or barrier may be present at birth while for others it may be acquired as a result of normal growth and maturation;

3. That either malnutrition or the absence from the diet of certain specific substances such as thiamin, riboflavin, and presumably others during the period of rapid growth may prevent or retard the appearance of at least some of the barriers to involvement of the nervous system by certain viruses.

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PUZZLES OF PROTEIN PRIVATION

A Decade of Research Into the Biologic Effects of Restricted Dietary Protein

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THIS afternoon I appear before the Society for Pediatric Research to inaugurate a departure from established routine. It would be a breach of candor not to state frankly my pleasure in launching a new project; namely, the presidential address. Particularly is this so since there has been no fetter of fashion, no course of custom, to shackle a roving imagination in quest of a suitable subject. Several months ago a note from an efficient secretary brought the fateful news that the years have been flashing by, that the present session is to be my last as an active member of the Society. The circumstance has dictated the choice of subject. Through a period of years which embrace the active Society membership, I have maintained an interest in the biologic effect of diets which contain too little protein. On sundry occasions the results of investigations have been brought to your attention; the fact that you have listened kindly and argued helpfully has provided continual motivation for pursuing fresh phases of study. It is fitting, therefore, to use this occasion for a fast journey through a decade of research in the field which furnishes continuity and contact with the Society.

The background for my interest in the subject of protein deficiency was provided by a period of residency in China from 1928 to 1930. The diet upon which the masses of people in North China subsist is composed largely of cereal grains, millet, and corn. Under favorable circumstances, particularly when native vegetables and the soybean are taken as supplements, the diet is just sufficient for the maintenance of health. In times of stress and when intercurrent disease, especially dysentery, complicates the picture, the diet becomes inadequate and deficiency diseases are widespread. Among these the most prevalent is nutritional edema; the edema is not infrequently associated with anemia, keratomalacia, and occasionally beriberi. It is of passing interest to observe that a situation similar to that in China exists today in a region much nearer home. In Puerto Rico the native islanders subsist largely on rice and beans. When I visited there two months ago, I found severe nutritional edema in all of the hospitals, and often other deficiencies, ariboflavinosis and pellagra, were superimposed.

From the Department of Pediatrics, College of Physicians and Surgeons, Columbia University.

Presidential address at the Thirteenth Annual Meeting of the Society for Pediatric Research, Atlantic City, May 6, 1941.

Fig. 1 will call to mind a series of observations on children with nutritional edema made during my days in China. The three columns refer respectively to the albumin, globulin, and total protein of serum. The black dots show the concentrations in samples from subjects who exhibited edema; the open circles represent samples after treatment had been begun and edema had disappeared; the vertical lines in the middle of each column indicate the range of normal variation. With albumin, all edematous patients show concentrations considerably below the range of normal; between 2.5 and 3 Gm. per 100 c.c. a critical zone is apparent. Edema is not observed when the albumin is greater than 3 Gm. per cent and is generally present when the albumin is less than 2.5 Gm. per cent. With globulin, the same range of concentrations above and below normal is observed both in edematous and in convalescent subjects. With total protein, the rough critical zone in the neighborhood of 5 Gm. per cent obviously results from variations in the albumin component. These observations were made on hospitalized patients. Later experience has taught that the same critical zones are not observed with ambulant subjects.

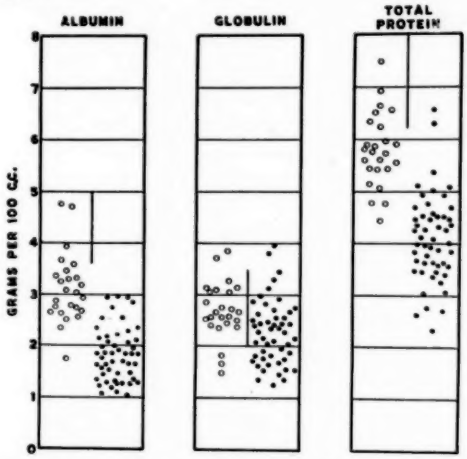

Fig. 1.—Summary of seventy-seven observations of the serum proteins on twenty-eight patients with nutritional edema. The black circles refer to estimations made while edema was still present; the open circles indicate determinations after the disappearance of edema. The vertical lines in the middle of each column show the range of normal variation. (From Weech: Internat. Clin. 2: 223, 1936.)

My first attempts to reproduce the disease in dogs were started in association with Dr. E. Goettsch at the Babies Hospital in 1931. After a number of trials, a suitable low-protein diet, composed chiefly of carrots, rice, lard, and sugar, was evolved. Dogs subsisting on the diet were in negative nitrogen balance. They exhibited a progressive fall (Fig. 2) in the concentration of albumin in the serum; the fall was initially rapid and later much slower. Average globulin concentration was virtually unaffected so that the fall in albumin was paralleled closely by

a similar decline in total protein. After periods which varied from forty to one hundred days, subcutaneous edema and sometimes ascites made their appearance. Fig. 3, which shows the serum protein findings

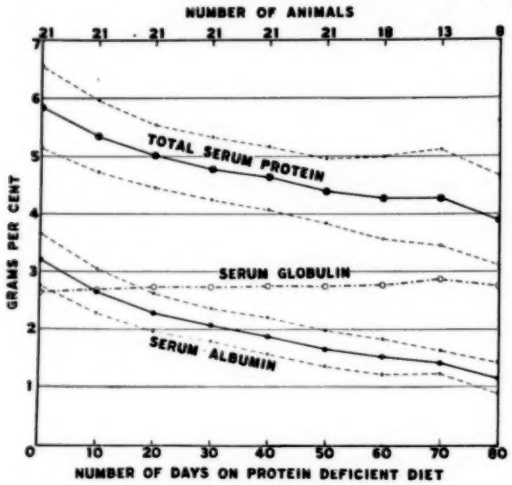
NUMBER OF ANIMALS
21 21 21 21 21 21 18 13 8
TOTAL SERUM PROTEIN
SERUM GLOBULIN
SERUM ALBUMIN
GRAMS PER CENT
0 10 20 30 40 50 60 70 80
NUMBER OF DAYS ON PROTEIN DEFICIENT DIET

Fig. 2.—The average trends of albumin, globulin, and total protein during maintenance on the low protein diet. The dotted lines above and below the unbroken lines for albumin and total protein are placed at a distance of one standard deviation from the average values. (From Weech, Goettsch, and Reeves: J. Exper. Med. 61: 299, 1935.)

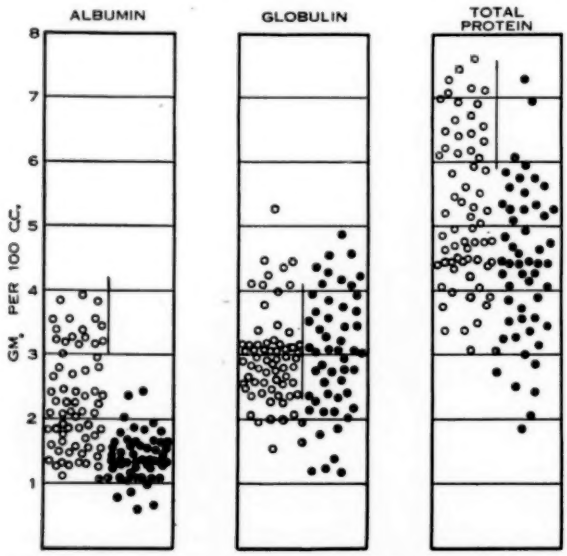

Fig. 3.—The relation between plasma-protein concentration and edema in dogs. Open circles indicate estimations when no edema was present; black circles refer to determinations after edema had developed. Vertical lines in the middle of each column show the range of normal variation. (From Weech, Snelling, and Goettsch: J. Clin. Investigation 12: 193, 1933.)

in a few of the earlier experiments, is similar to Fig. 1. Here the open circles and black dots refer respectively to analyses before and after edema had developed. The zone of albumin concentration critical for edema formation is between 1 and 2 Gm. per cent; that is, it is lower than the critical zone of children with nutritional edema. Globulin concentrations are even more erratic with dogs than with children, and the total protein column discloses such wide variability that a critical zone cannot be defined.

We have here then in outline an experimental method applicable for studying a number of aspects of protein deficiency and edema. Some of the aspects which have already received attention can only be mentioned and others will have to be omitted since I must save time for those who will follow on our program. An early step was to exclude the role of accessory vitamin deficiency in producing the hypoproteinemia and edema. We can state now that these symptoms are not prevented by the liberal administration of cod-liver oil, rice-polishing extract, and Lilly's No. 343 liver extract. Of collateral interest was the finding that many of the dogs develop, and may succumb to, peptic ulcer; the ulcers cannot be prevented by the vitamin supplements.[1]

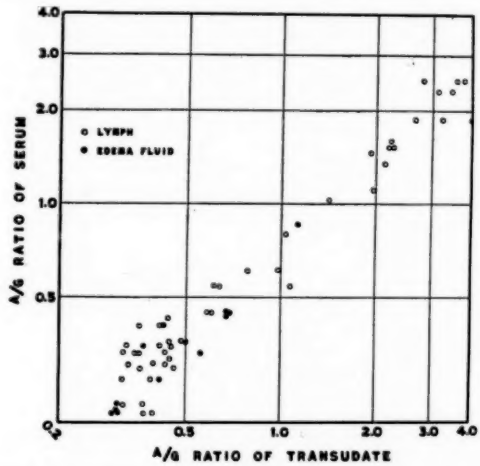

Fig. 4.—The relation between the albumin-globulin ratios of concurrently collected samples of serum and transudate. (From Weech: *Harvey Lecture,* Bull. New York Acad. Med. 15: 63, 1939.)

In other experiments animals with nutritional edema were used to study the influence of lymph flow and lymph composition on the formation of edema.[2] Samples of lymph and edema fluid obtained during this work were analyzed for albumin and globulin. Some of these findings are presented in Fig. 4 in such a way that the A:G ratio of serum can be compared with the A:G ratio of the transudate. The fact that the analytical points fall along a line strongly supports the

concept that the albumin and globulin of lymph and edema fluid originate by filtration from the plasma. It also can be seen that the transudate ratio is invariably a little greater than the serum ratio. This means that the capillary wall is somewhat more permeable to the smaller albumin molecule than to the larger globulin molecules.

I have included Fig. 4 chiefly because out of the work which it presents came a more important finding. It is not easy to analyze transudates accurately for albumin and globulin; to obtain the desired precision, Dr. Goettsch turned to the quantitative precipitin reaction, an immunologic procedure made available through the fundamental work of Heidelberger and Kendall. Later she attempted to apply the method to samples of serum and edema fluid from children with nephrosis. And so it was learned[3] that the serum proteins in this disease are altered from normal in a way which can be assessed quantitatively by the precipitin technique. This finding subsequently has been confirmed in another laboratory by a wholly different technique of approach; namely, by the use of the Tiselius electrophoresis apparatus.[4]

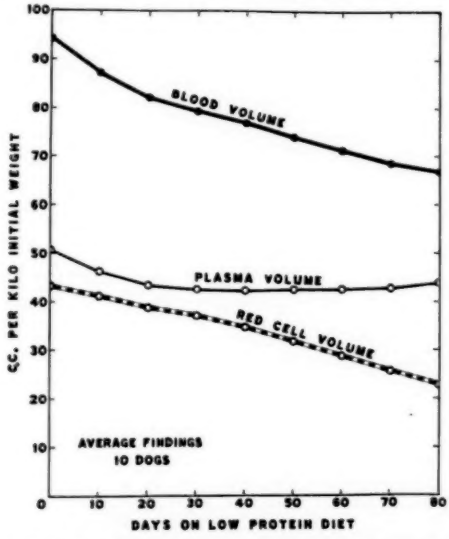

Fig. 5.—Changes in blood volume, plasma volume, and red cell volume during maintenance on the low protein diet. (From Weech, Wollstein, and Goettsch: J. Clin. Investigation 16: 719, 1937.)

Another phase of these investigations has dealt with the changes in blood volume which accompany maintenance on the protein-deficient diet. The average findings in ten dogs are shown in Fig. 5. There is a continuous decline in red cell volume and in total blood volume during the eighty-day period. The circulating plasma shows an initial rapid fall to a volume which is then maintained for the duration of the experiment. Because the early decreases affect both plasma and erythrocytes, the usual red cell counts and hemoglobin determinations fail to

record the progressive loss from the circulation. The fact that plasma volume does not continue to decline throughout the experiment does not mean that at the later stages it is no longer sensitive to change in albumin concentration. It means merely that another limiting factor, total blood volume, has come into play. Both from data of this type and from experiments in which hypoproteinemic dogs have been transfused with normal serum, it has been shown[5] that plasma volume is always affected by the concentration of serum albumin. The knowledge has helped in the clinic by providing a rational explanation for the rapid changes in red cell count and hemoglobin level which always accompany shifts in the serum albumin.

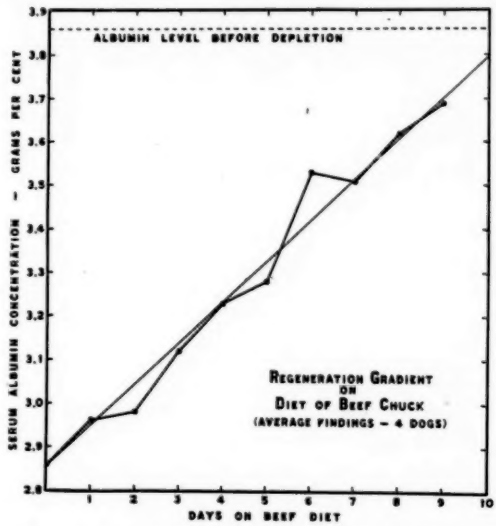

Fig. 6.—The average results for four dogs of determinations of serum albumin concentration during regeneration on a diet which furnished 5 Gm. of protein per kilogram. The added protein was in the form of beef muscle (chuck). (From Weech and Goettsch: Bull. Johns Hopkins Hosp. 63: 154, 1938.)

Because the deficit in serum albumin is one of the very important results of protein deficiency, attention has been paid not only to the curve which describes progressive depletion but also to the course of regeneration when adequate feeding is resumed. When the experiment has been brief and the albumin deficit is moderate, the institution of adequate feeding results in regeneration which varies in rate both with the amount and with the quality of the protein in the diet. Fig. 6 shows the path of replenishment when the diet contains 5 Gm. of beef protein per kilogram of dog weight. The essentially linear nature of the regeneration curve indicates that a fixed amount of the diet is being utilized each day for the fabrication of albumin. There is no evidence to suggest that the amount used for this purpose depends upon the extent of the albumin depletion. This circumstance has made possible

the realization of another objective; namely, the use of the standardized hypoproteinemic dog as a means of assaying various food proteins with respect to their ability to promote the formation of serum albumin.

The assays involve measurement of the increment in albumin concentration during a week when the food protein to be tested is fed in standardized amounts. Because among different animals the range of biologic variation is wide, a series of tests must be made before an average assay value, which we have termed the "potency value," can be assigned to a food.

TABLE I

RELATIVE EFFICIENCY OF DIFFERENT PROTEINS FOR SYNTHESIS OF SERUM ALBUMIN

SOURCE OF FOOD PROTEIN	POTENCY VALUE	NUMBER OF ASSAYS	PROBABLE ERROR
Beef serum (fresh)	0.801	11	0.053
Beef serum (all assays)	0.770	22	0.030
Lactalbumin	0.768	16	0.028
Beef serum (dried)	0.739	11	0.029
Egg white	0.616	11	0.023
Cow colostrum	0.611	9	0.042
Egg (all assays)	0.608	23	0.020
Egg (whole)	0.602	12	0.033
Milk	0.483	11	0.021
Beef chuck	0.475	12	0.021
Beef liver	0.445	11	0.025
Casein	0.425	21	0.022
Wheat gluten	0.207	7	–
Gelatin	–0.093	4	–

The food proteins tested so far are listed in Table I; they are given in descending order of potency and are arranged in four groups. In general, the proteins in any one group differ significantly in effectiveness from the proteins in each of the other groups, but within one group the order of the several foods is not established with certainty. Thus, beef liver is clearly less potent than the proteins in the first two groups and more effective than wheat gluten and gelatin which comprise the last group. Fresh beef serum with a potency value of 0.801 is at the head of the list. Because it is difficult to prepare and preserve fresh serum in a form suitable for food, our attention turned to the possible usefulness of dried serum.* The effectiveness of the dried beef serum is represented by a potency value of 0.739, a figure which does not differ significantly from that of fresh serum. Accordingly the entire series of assays of serum have been combined to yield a potency value of 0.770. Unfortunately, I have to report that the dried serum at our disposal possesses an unpleasant and lingering flavor which has defied disguise by the arts of seasoning and cooking. Dogs love it, but children exhibit a singular lack of enthusiasm. The high potency of lactalbumin was found less than a year ago. Conferences with Dr. Supplee,

*We are indebted to the Armour Packing Company for manufacturing a generous supply of this material.

of the Borden Company Research Laboratories, indicate that it is possible to produce this protein in a soluble form suitable for food purposes. New preparations of the soluble lactalbumin are being used now in feeding experiments conducted on the ward. The lactalbumin previously available had been prepared from milk whey by the simple expedient of heat coagulation. The dry product was insoluble and gritty. The new preparation is soluble and readily miscible with water and milk, a property which has been obtained by an appropriate balance of the hydrogen-ion concentration and the ionizable mineral content. The new preparation contains about 3 per cent ash and has a hydrogen-ion value of approximately 6.8.

Before leaving this list of foods I must invite your attention to the interesting properties of colostrum milk.* The first colostrum from cows contains from 12 to 16 per cent of protein and, like the white of egg, it coagulates on boiling. Because it contains more albumin and globulin than casein, we entertained the thought that it might possess a potency value like that of beef serum. The potency value of 0.611 is about what would be expected if colostrum were a mixture of ordinary milk and beef serum.

And now to a final point which will introduce a phase of this work which is currently under investigation. Accumulating evidence indicates that the synthesis of serum albumin depends not only on a supply of proper food but also on normal functioning of the organs responsible for the synthesis. Presumably the principal organ concerned is the liver. Patients with cirrhosis of the liver usually exhibit serum albumin depletion; often the deficits are not affected by treatment with diet. Likewise no diet has been discovered which is invariably effective in influencing the low albumin levels of patients with nephrosis; these patients may suffer from defect in the synthesizing mechanism. Finally, in chronic cases of nutritional edema, the low serum albumin is sometimes refractory to treatment with diet. Obviously, then, the benefit from dietary therapy can be limited by the ability of the body to utilize the nutritional elements. And since a better understanding of the mechanism for synthesis may conceivably open the way for a new type of treatment, our attention has turned to the study of liver function in the protein-starved dog. Previous experience had led to the suspicion that the livers of these animals might not function normally. Slowly developing carotinemia suggested a defect in the function of transforming carotin into vitamin A. In the terminal stages many animals showed an increase in serum bilirubin and at autopsy there was often excessive infiltration of the liver with fat.

Fig. 7 depicts the course of events in a dog which was maintained for twenty-one weeks on the low protein diet and in which bilirubin-

*The colostrum for our assays was obtained through the cooperation of the Walker Gordon Milk Company; each sample was collected within 6 hours of the time of calving.

clearance measurements were made at repeated intervals. The usual curve of declining serum albumin was reproduced by this animal except that the rate of fall was slower than in most instances. The behavior of liver function is shown by the heavy line, the measure being the velocity of bilirubin clearance in milligram units $\times 10^{-3}$.[6] During the control period the velocity of excretion was relatively constant between 17 and 18 units; after only six days on the deficient diet the velocity had fallen to 14.3 units. Thereafter we noted a progressive fall in the ability of the liver to excrete bilirubin until about thirteen weeks had elapsed. At this low point the excretion velocity was only 2.4 units. Then, as is often the case in biologic experiments, something unexpected happened; liver function improved during a period when ascites, which ultimately became massive, was accumulating. I shall not, cannot, explain this happening and am able only to comment that the riddle which it poses is one of those things that enhance the fascination of biologic research.

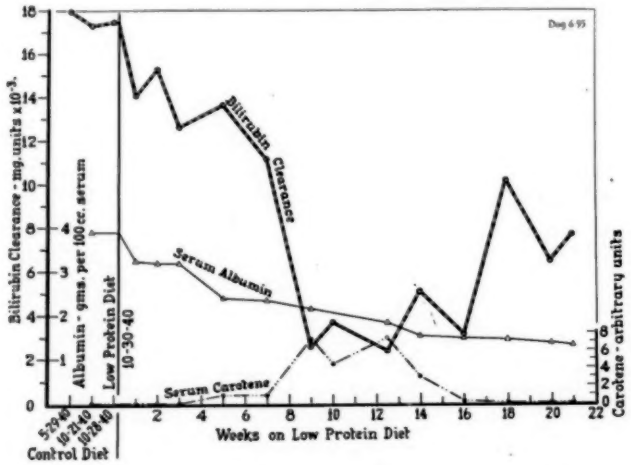

Fig. 7.—The effect on the function of the liver of continued maintenance on the low protein diet. The test of hepatic function, based on the capacity of the liver to excrete bilirubin, has been described in the J. Clin. Investigation **20**: 323, 1941. The parallelism between bilirubin clearance and the concentration of carotin in the serum depends on associated change in the power of the liver to convert carotin into vitamin A.

The bottom line on the chart shows the course of serum carotin concentration. The carotin level rises when the ability of the liver to excrete bilirubin falls, and it declines when the excretory function shows its unexpected improvement. Under these conditions of constant food intake, then, carotin concentration has furnished another measure of the function of the liver.

The work in this field is obviously incomplete. I doubt indeed that we are even in sight of the end. Bilirubin clearance and carotin concentration may furnish a suitable yardstick of ability to fabricate

albumin; perhaps again they may not and other tests will have to be devised. But the goal will not have been attained until a yardstick can be used to appraise therapy, therapy aimed at restoring the power of the liver to synthesize albumin.

In conclusion, I should like to express a hope that some member of this research society may have been intrigued by this puzzle of protein privation and may in consequence thereof choose to join the chase of an alluring but elusive solution.

The occasion for which the foregoing address was prepared and the limited time for presentation rendered it impossible to include a review of pertinent literature. In releasing the manuscript for publication an attempt has been made to make amends for inability to mention the contributions of other investigators by adding a list of references. Some of these are given in the legends which accompany the charts; some are listed in the references. In them due acknowledgment is made of the work of others. It is also wished to take this opportunity to express thanks to the Committee of the Williams-Waterman Fund for the Combat of Dietary Diseases who have contributed generously to the support of these investigations during the past year.

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STUDIES ON MENINGOCOCCUS INFECTION

NELLES SILVERTHORNE, M.B., AND COLIN CAMERON
TORONTO, ONT.

INTRODUCTION

IN 1939, we published a review[1] of 51 cases of meningococcus infection in children occurring between 1931 and 1938. In addition to brief references to the literature, clinical, bacteriologic, epidemiologic, and other observations concerning this infection were recorded. From January, 1938, to April, 1941, fifty-nine cases have been admitted to the Hospital for Sick Children, Toronto. Certain features of the infection have differed from the cases previously reported, and observations on other aspects of the disease have been made. This communication will record certain clinical and laboratory studies which may be significant in the evaluation of treatment.

Clinical Data.—From January, 1938, to April, 1941, there have been 59 patients with meningococcus infection admitted to the hospital. The meningococcus was isolated from the blood or cerebrospinal fluid in all patients. In some instances the meningococcus was cultured from both blood and spinal fluid. In this series of 59 patients, 3 distinct clinical forms of the disease were seen. Three patients were of the fulminating type, 50 were suffering from the acute meningeal form, and 6 patients were bacteremic cases without meningeal involvement. Twenty-three of the fifty-nine patients had hemorrhagic rashes. Four patients presented a fine diffuse macular rash, simulating German measles, a few days prior to the meningeal signs. The patients were treated by one of three different methods: (1) Nine patients received polyvalent antimeningococcus serum intravenously and intrathecally; (2) nine patients received sulfanilamide or sulfapyridine; (3) thirty-seven patients received polyvalent antimeningococcus serum intravenously and intrathecally as well as sulfanilamide or sulfapyridine. These drugs were given by mouth, and in some instances intravenous forms of the drugs were used as the initial dose. In the serum-treated group there were two deaths; in the drug-treated group, no deaths; and in the serum- and drug-treated group, six deaths. There was no time available to treat three patients with the fulminating disease who died shortly after admission. One patient was admitted with a meningococcemia without meningeal involvement, received no treatment, and made a rapid recovery. Reference to this patient will be made later. Table I shows the case fatality with reference to treatment. Another interesting fact is seen from a perusal of the fatality rate of the clinical types of the disease in Table II. The three patients with the fulminating disease all

From the Wards and Laboratories of the Hospital for Sick Children and the Department of Paediatrics, University of Toronto, under the direction of Alan Brown, M.D., F.R.C.P. (Lond.), and from the Connaught Laboratories, University of Toronto.

TABLE I

MENINGOCOCCUS INFECTION

NUMBER OF PATIENTS	TREATMENT	DEATHS	CASE FATALITY (%)
9	Serum	2	22
37	Serum + Drug	6	16
9	Drug	0	0
3	None	3	100
1	None	0	0
59		11	18.6

TABLE II

MENINGOCOCCIC INFECTION

Clinical Data

TYPES	NUMBER	RECOVERED	DIED	CASE FATALITY (%)
Fulminating	3	0	3	100
Acute meningeal	50	42	8	16
Bacteremic	6	6	0	0

died, a case fatality rate of 100 per cent. The fifty acute meningeal types showed a fatality of 16 per cent, whereas the purely bacteremic types, six in number, recovered. This table shows that the prognosis varies with the clinical type of the disease. Treatment had very little to do with the variation in the case fatality rate in the acute meningeal and bacteremic patients because they were treated in much the same manner except for one bacteremic patient who did not receive any treatment.

Age.—The ages of the patients varied from 24 days to 11 years. The 24-day-old infant recovered. Brown and Silverthorne[2] reported the recovery of a 22-day-old infant some years ago. This infant received polyvalent serum intravenously and intrathecally on the first day of the disease.

Sex.—Of the 59 patients, 35 were male and 24 were female.

Monthly Incidence.—In Fig. 1 will be seen the number of cases occurring during the various months of the year from January, 1938, to April, 1941. During the years 1938 and 1939 a few sporadic cases occurred. In 1940 and in the early part of 1941 there was a definite increase in the number of cases.

CASE REPORT

One patient in this series is of special interest on account of the fact that the child had a meningococcemia, received no specific treatment, and made a rapid recovery. In addition, studies on the bactericidal power of his blood revealed significant findings. The patient, L. B., male, aged 3 years, was admitted in October, 1939, with a complaint of headache, fever, vomiting, drowsiness, and a skin eruption for 3 to 5 days. The family and past histories were irrelevant. In the hospital the infant had a high fever with a chill, appeared acutely ill, was drowsy, and had a profuse hemorrhagic rash. He received only fluids by mouth, and in twenty-four to forty-eight hours after admission he became much brighter and

sat up in bed. His blood culture on admission grew the meningococcus, although his cerebrospinal fluid was clear and was sterile on culture. During his stay in the hospital, the bactericidal power of his blood was tested on the third, fourth, fifth, sixth, and seventh days after admission. The test for determining the bactericidal power of blood was set up as previously reported.[4] Table III indicates the results of these tests.

TABLE III

BACTERICIDAL EFFECT OF PATIENT'S BLOOD ON PATIENT'S STRAIN OF MENINGOCOCCUS

"B" BLOOD	"B" CULTURE DILUTIONS					
	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}
1st hospital day	+	+	+	+	+	+*
2nd hospital day	No blood examined					
3rd hospital day	+	+	−	−	−	−
4th hospital day	+	−	−	−	−	−
5th hospital day	−	−	−	−	−	−
6th hospital day	−	−	−	−	−	−
7th hospital day	−	−	−	−	−	−

*Usual finding
+ = Confluent growth
− = No growth
10^{-1} = Approximately 2,000,000 meningococci
10^{-6} = Approximately 20 meningococci

The blood culture of this patient was positive on his first day in the hospital during the time the hemorrhagic rash was present. A sample of blood for bactericidal action was not taken on his first hospital day. In the examination of blood samples for bactericidal power in other cases we have found no bactericidal power in the blood in the early stage of the disease when the blood culture is positive. This finding is indicated in Table III. However, as revealed in the table, samples of blood from the third to the seventh hospital day show a rise of bactericidal power in his blood against his own virulent strain (10^{-7} in mice). These interesting findings will be discussed in the general discussion.

Pathologic Data.—The only data of interest to record in this series is the finding of the Waterhouse-Friderichsen syndrome in two of the fulminating cases. Both patients had a meningococcemia, multiple petechiae over the body, and massive hemorrhages into both adrenals. One patient had an early meningitis.

Virulence of Strain.—In addition to the usual tests of establishing the identity of strains of meningococci by methods previously reported,[1] virulence tests were done on strains obtained from blood or cerebrospinal fluid of patients. All strains showed some degree of mouse-mucin virulence when they were tested with the technique reported by Rake.[5] The virulence of these strains varied from 10^{-5} to 10^{-8}. In order to compare the virulence of strains with the severity of the disease in the patients, strains from thirty-eight patients classified clinically as severe, moderately severe, and mild were examined for mouse-mucin virulence. Table IV summarizes the results.

From the table it will be observed that of the 17 severe types, 8 strains showed a mouse-mucin virulence up to 10^{-8} (20 meningococci), 2 strains, a virulence of 10^{-7}, 3 strains, a virulence of 10^{-6}, and 4 strains, a virulence of 10^{-5}. There were 15 moderately severe clinical cases: 2 of these patients had strains of 10^{-8} virulence, 5 had strains of 10^{-7} virulence, 6

TABLE IV

COMPARISON OF CLINICAL SEVERITY OF MENINGOCOCCIC INFECTION WITH VIRULENCE OF STRAINS

NUMBER OF PATIENTS	CLINICAL SEVERITY	NUMBER OF STRAINS ACCORDING TO VIRULENCE*			
		10^{-5}	10^{-6}	10^{-7}	10^{-8}
17	Severe	4	3	2	8
15	Moderately severe	2	6	5	2
6	Mild	2	4	0	0

*Number of meningococci in mucin used to kill mice
10^{-5} = Approximately 20,000 meningococci
10^{-8} = Approximately 20 meningococci

had strains of 10^{-6} virulence, and 2 had strains of 10^{-5} virulence. Of the 6 mild clinical cases, 4 patients had strains of 10^{-6} virulence and 2 had strains of 10^{-5} virulence. Although there is no absolute evidence that the virulence of strains in mice corresponds to the severity of the disease in patients, Table IV does indicate that in certain instances the more severe the clinical disease, the more likely is the culture to be of higher virulence and vice versa. L. B., the patient who received no specific treatment and who developed bactericidal power in his blood and recovered, had a blood culture strain of a virulence of 10^{-7}. This child was classified as moderately severe clinically although he did recover very quickly. This observation suggests that the immunity mechanism of the host is possibly more important in the recovery of the patient than the mouse-mucin virulence of the strain. It must be remembered, however, that the virulence of infecting strains likely does play a definite role in the recovery of certain patients and thus the proper evaluation of the virulence of strains should be done before deciding the value of the treatment in each case.

Blood Bactericidal Data.—Blood bactericidal tests were carried out as previously reported.[4] Samples of blood were obtained from 13 patients. Several samples were tested from each patient. Ten of the thirteen patients showed the development of bactericidal power in their blood. Of these 10 patients, 4 had received sulfanilamide only; 2 sulfapyridine only; 2, serum only; 1, sulfanilamide and serum, and 1, L. B., no treatment. Two patients did not show the development of bactericidal power in their blood, and one patient developed it during the course of treatment but the blood became less bactericidal on the day of death. From these results it is likely that the development of blood bactericidal power during the course of meningococcus infection has something to do with the recovery of the patient. It is not assumed, however, that the rise of bactericidal power is the only immunity mechanism associated with recovery. It is freely admitted that there may be other mechanisms. It was noticed from our tests that specific therapy did rapidly enhance the development of bactericidal power and this fact as well as the encouraging results from clinical use of the drug justifies the use of specific agents (e.g., drugs or serum or both).

Typing of Meningococci.—Typing was done as described in a previous article[1] (method b). Of 72 strains typed from 1936 to April, 1941, 28 were Group I, 30 were Group II, and 14 showed cross agglutination to such an extent that they could not be classified by this method of typing. In our report in 1939[1] we suggested that Type II meningococcic infections in children were sporadic and that Type I infections were likely associated with epidemic forms of the disease. In Fig. 1 it will be observed that in 1938 and 1939 the disease was sporadic in children. From Fig. 2 one observes that from 1936 to 1938 the disease was mostly due to Group II meningococcus. This fact was previously reported.[1]

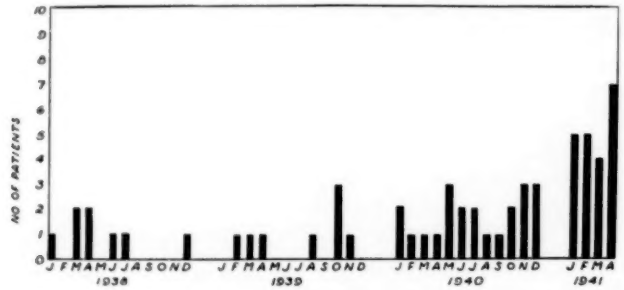

Fig. 1.—Monthly incidence of meningococcus infection among children at the Hospital for Sick Children, Toronto, Ont., January, 1938, to April, 1941.

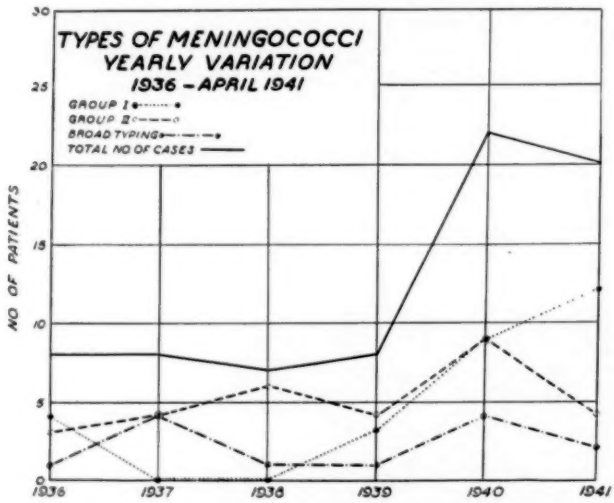

Fig. 2.—Yearly variation in types of meningococcic between 1936 and April, 1941.

In Fig. 1 it will be seen that not only has there been an increase in the total number of patients with meningococcus infection in 1940 and 1941, but in 1940 (Fig. 2) there has been an increase of both Group II

and Group I infections. Group I infections were absent in our series in 1937 and 1938 but began to appear in 1939 and 1940. As the incidence of cases increased per month in 1941 (Fig. 1), the number of Group II strains decreased and the number of Group I strains increased (Fig. 2). This observation seems to confirm our previous contention that Type II strains are prevalent in sporadic times, whereas Group I strains are associated with epidemics. Although for the most part strains of meningococci fall into the Group I or Group II classification, certain strains show cross agglutination. Occasional strains have been shown to be Group I in absorbed sera and Type II in unabsorbed typing sera. In certain instances we have obtained results such as are seen in Table V.

TABLE V

TYPING OF MENINGOCOCCI WITH SERUM

SERUM	1:20	1:40	1:80	1:160	1:320	1:640
Type I	1	½*	0	0	0	0
Type II	3	2	1	0	0	0
Group I	4†	4	4	3	3	3
Group II	0	0	0	0	0	0

*½ = Trace of agglutination
†4 = Complete agglutination with water-clear supernatant

Although there is cross agglutination in the typing with type sera, the indication is that the strain is Type II, whereas it appears to be a Group I strain (i.e., Types I and III) in the group sera. The type sera were obtained from rabbits which had been inoculated with freshly isolated strains collected in the last few years, and in the latter case the sera were obtained from rabbits inoculated with standard strains Group I (Types I and III) and Group II (Types II and IV), and the sera were reciprocally absorbed. Recently we reported[6] on the classification of pathogenic meningococci by their ability to survive in the blood of normal guinea pigs. Strains were set up with samples of blood from normal guinea pigs in the bactericidal test, the technique of which was previously described.[4] It was found that the ability of meningococci to survive in samples of blood from normal guinea pigs clearly differentiated the strains into two groups which, for the most part, showed the following differentiation (see Table VI). From Table VI it would appear that clearer differentiation of strains may be made by the ability of meningococci to survive in samples of blood from normal guinea pigs since there is rarely any tendency to overlapping as is seen in the cross agglutination of strains by the method of typing by serum agglutination. The 19 Group I strains did not survive and the 17 Group II strains survived to the limiting dilution of the test. The 5 strains that cross agglutinated in the method of typing with sera survived in guinea pig blood and in this respect behaved as Group II strains. The 2 strains that cross agglutinated in the method of typing with sera did not survive in guinea pig blood and in this respect behaved as Type I strains.

In a recent experiment this difference in the survival of Type I from Type II strains of meningococci in samples of blood from normal guinea pigs appears to be due to the fact that there is more natural bactericidal power in the blood of normal guinea pigs to Type I strains than to Type II strains. Details of these experiments will be published at a later date.

TABLE VI

TYPING OF MENINGOCOCCI

NUMBER OF STRAINS	TYPES BY AGGLUTINATION	SURVIVAL IN NORMAL GUINEA PIG BLOOD DILUTIONS OF MENINGOCOCCI				
		10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}
19	Group I (Types I and III)	±	−	−	−	−
17	Group II	+	+	+	+	+
5	Cross agglutination	+	+	+	+	+
2	Cross agglutination	±	−	−	−	−

− = No growth
+ = Confluent growth
10^{-1} = Approximately 2,000,000 meningococci
10^{-3} = Approximately 200 meningococci

DISCUSSION

Certain features of our clinical and laboratory studies merit discussion. In a report on meningococcus infection published in 1939[1] which reviewed 51 cases of this disease occurring over a seven-year period between 1931 and 1938, it is noteworthy that all had meningeal involvement. The patients were classified as fulminating (6 cases), acute (40 cases), and chronic basilar (5 cases). In the present series, the 59 patients may be divided into fulminating (3 cases), acute meningeal type (50 cases), and bacteremic (6 cases). The present series differs from the former in that there were 6 bacteremic cases with no meningitis. These patients showed a tendency to more rapid recovery than those with meningeal involvement. In the present series there were no chronic basilar types unless one of our patients at present in the hospital is developing a chronic basilar lesion. If the results of treatment are examined in Table I, it will be observed that nine patients receiving drugs recovered. In the 9 serum-treated patients there were 2 deaths, and in the 37 drug- and serum-treated patients there were 6 deaths. Two patients of this last group with Group I infections received six to eight days' treatment with drugs and serum intravenously. They required intrathecal serum before sterilization of the spinal fluid occurred although both patients had levels of the drug as high as 9 mg. per cent in their spinal fluids. Hoyne, in a recent article,[3] does not believe in the use of intrathecal serum. The elimination of the intrathecal method of serum treatment may be justified in many instances; yet in these patients we believe that the use of intrathecal serum played a definite role in their recovery. The one patient, L. B., with a bacteremic type of the disease who did not receive drugs or serum made a rapid recovery.

We believe that if this child had received specific therapy, we would have claimed that the treatment was the curative factor. Certain patients arrived at the hospital so critically ill that a bad prognosis was obvious irrespective of the specific form or forms of therapy instigated. Three patients of the fulminating type died before any treatment could be administered. Others died having received supposedly adequate amounts of drug and serum. From these observations it must be evident that prognosis differs not only with the different clinical types of the disease, but also within the same clinical type. Thus, clinical factors must of necessity enter into the proper evaluation of the results of therapy. As well as clinical variations in the disease, other factors enter into the final outcome of each patient.

It has been shown previously that different bacterial types are associated with the disease at different periods, and therefore it is advisable to have facilities at hand for typing each strain. McLeod[7] and Branham[8] in a recent publication have shown how important in treatment is the knowledge of types. This is especially true, since we believe that Type II infections are, on the whole, associated with the sporadic occurrence of the disease and that Group I infections are likely prevalent as the disease increases in its incidence during epidemic times. These suggestions are rather well borne out by the fact that during our sporadic years, Group II was prevalent, and as the disease increased in number of patients in 1941, Group II infections decreased relatively in number and those of Group I increased (Fig. 2). It has been shown that although each strain has some degree of virulence when injected with mucin into mice, there is a definite variation in this virulence (from 10^{-5} to 10^{-8} dilution of the meningococcal suspension). This also must be a factor in the evaluation of treatment. We have observed patients with a very mild infection who we judged would recover in spite of treatment. The infecting strains in some of these instances have had a comparatively low mouse virulence (10^{-5} or 10^{-6} dilution of the meningococcal suspension) (Table IV).

Another factor certainly must be the immunologic response of each patient. Although we do not believe that the development of bactericidal power in the blood of the patient is the one and only mechanism, it has been shown to be associated with the recovery of the patient reported (L. B.). It is quite conceivable that, if the patient had received drug or serum, he would have been included in a series showing the beneficial results of these agents. In addition, we have shown in other publications[1, 4, 9, 10, 11, 12] that the rise of bactericidal power in the blood is associated with immunity to and recovery from meningococcal infection.

A discussion of various forms of treatment, however, is important. No one will doubt the advances made in the treatment of this disease by specific serum, and in recent years by drugs. Certainly, most clinics show a reduced case fatality after the use of sulfanilamide or sul-

fapyridine and in some instances with both drugs and serum. Our series is too small to offer any definite answer to the question as to whether drug alone, serum alone, or both drug and serum is the best form of treatment. However, we do not believe such questions can be answered accurately at present, largely due to other factors in the disease that have been discussed. Certainly, we have not reached the stage where we believe there is any panacea in the treatment of this infection. We have, however, followed a definite course of treatment which we believe to be beneficial to the patient, both in a specific and in a general way. At present, we believe that each patient suffering with meningococcal infection should receive as soon as possible (a) a continuous intravenous injection of glucose-saline, (b) an initial intravenous form of either sulfanilamide or sulfapyridine followed by 1½ to 2 gr. of the drug per pound per day by mouth, (c) intravenous and intrathecal polyvalent antimeningococcus serum of high agglutinating and mouse protecting potency, (d) a blood transfusion when the hemoglobin is diminished, and (e) daily lumbar puncture with drainage until at least three successive spinal fluids are sterile. We do not believe that initial examination of spinal fluid is all that is required. We believe that the daily examination of the spinal fluid for culture and drug estimation is very important, and in addition, the drainage of spinal fluid is in keeping with one of the first principles of the surgery of any infected focus. Certainly, the best criterion for a good prognosis with almost all forms of purulent meningitis is repeatedly sterile spinal fluid cultures. The daily estimation of the drug in the spinal fluid gives information as to whether or not enough drug is being administered. If one examines the case fatality rate in our first series of patients previously reported[1] and the present series, one finds that in both groups the patients with the fulminating disease die before any treatment can be made available. The case fatality rates in the acute meningeal types of the disease of both series show that in our first report[1] the patients were treated exclusively with polyvalent anti-meningococcic serum and the case fatality was 14 per cent. In the present series, there were thirty-seven patients treated with drug and serum, resulting in a case fatality rate of 16 per cent. In other words, there is practically no difference in the outcome of these groups of the acute meningeal type treated with different materials. It would appear from this evidence that other factors than treatment likely have a very important effect on recovery from this disease.

SUMMARY

In this report we have attempted to review some of the aspects of meningococcus infection which may have a very definite bearing on the evaluation of treatment. The points to be considered are variations in clinical type, variations in prognosis with the same clinical type, variations in virulence and type of infecting strains, the mechanism of im-

munity response in patients, and finally, the treatment instigated. All these aspects of the disease should be properly evaluated before too many far-reaching claims are made solely on the basis of newer methods of treatment.

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SPOT MAPS OF BACILLARY DYSENTERY AND OF POLIOMYELITIS

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ALBERT M. PRICE, M.D., CHARLESTON, W. VA.

THE distribution of the child population in the city of Huntington, W. Va., is shown in a copy of a spot map (Fig. 1) prepared by the Cabell County Board of Education in 1937.

The distribution of cases of measles reported to the health department of the city of Huntington during the months of March and April, 1941, is shown on a second map (Fig. 2). It is noteworthy that the distribution of cases of measles is very similar to that shown for the school population. Particular attention is drawn to the fact that the central, heavily populated, and heavily built-up sections of the city were visited to an equal degree with that of the outlying areas. Infections spread in the main by respiratory discharges generally follow this pattern of distribution. This has been observed repeatedly in epidemics of measles and influenza in these same districts.

The distribution of dysentery cases for the period 1921 to 1931 is represented by a map (Fig. 3) which has been presented previously. Districts known to lack those sanitary protections which tended to hinder the spread of intestinal diseases by flies and otherwise had the highest incidence of cases of acute bacillary dysentery. These same districts have in general, but not invariably, the least adequate housing facilities, least favorable economic status, and least enlightened individuals. It is noteworthy that the central district, although heavily populated, has regularly presented few cases of dysentery. By contrast with the distribution of measles, this is worthy of note.

In 1927 Dr. Byrd Hunter drew attention to the similarity between the dysentery map (Fig. 3), then in progress of development, and the distribution of cases of paralytic poliomyelitis observed in the epidemic of that year (Fig. 4). His suggestion was given little favorable consideration by the three of us working with him, although we admitted the obvious similarity. The distribution of the forty-seven cases of paralytic poliomyelitis occurring in 1927 is shown in Fig. 4.

In the epidemic of poliomyelitis of 1940, forty-five cases of paralytic and sixteen cases of nonparalytic poliomyelitis were reported to the health department of the city of Huntington. The distribution of the cases is shown in Fig. 5. The pattern of distribution was the same as in 1927 and very similar to the dysentery spot map of 1921 to 1931.

Presented at the meeting of the American Pediatric Society, Hot Springs, Va., May 24, 1941.

In another map (Fig. 6) the places of residence of the poliomyelitis patients for both epidemics is shown (forty-seven paralytic cases in 1927, forty-five paralytic cases in 1940, and sixteen nonparalytic cases in 1940). The pattern of distribution, observed in both the 1927 and 1940 poliomyelitis epidemics, is quite similar to the distribution of bacillary dysentery for the years 1921 to 1931.

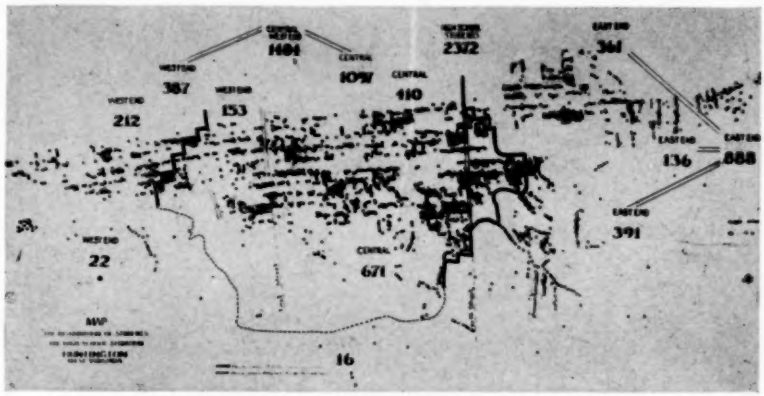

Fig. 1—Distribution of high school children, Huntington, W. Va., 1937.

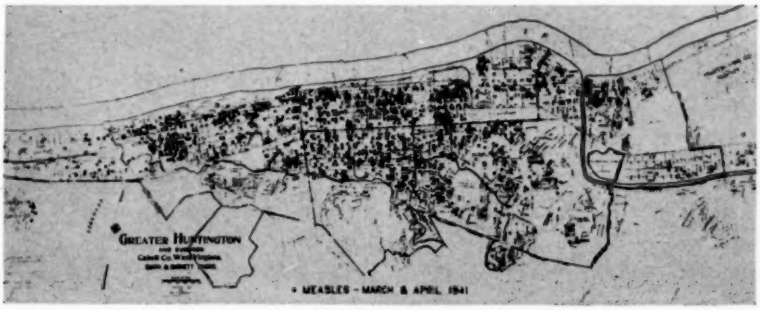

Fig. 2.—Distribution of cases of measles reported to the health department of the city of Huntington, W. Va., March and April, 1941.

The distribution of cases of poliomyelitis and of dysentery differed strikingly from that of measles in that the children living in the heavily populated central part of the city were not attacked with the same frequency as were those living in the marginal areas, whereas those living in the outlying districts had an excessive attack rate.

These observations suggest rather pointedly that the virus of poliomyelitis is not spread in the same manner as the virus of measles (by respiratory discharges). Furthermore, they suggest that the poliomyelitis virus and the bacteria responsible for bacillary dysentery are spread in the same manner (by intestinal discharges).

We believe these implications are sufficiently strong on their own account to encourage the development of investigations directed toward a study of the common house fly *(Musca domestica)* as a possible vector,

Fig. 3.—Spot map showing distribution and incidence of bacillary dysentery as observed in Huntington, W. Va., from 1921 to 1926 in children during the first five years of life. The open circles represent children seen in private practice who did not have dysentery, and the solid dots represent children seen in private practice who had dysentery. The open triangles represent children seen in the group from the Huntington Baby Welfare Clinic who did not have dysentery, and the solid triangles represent those from the clinic who had dysentery.

leading perhaps to the actual demonstrations of the importance of imperfectly protected stools and sewage as important factors in the epidemiology of acute poliomyelitis.

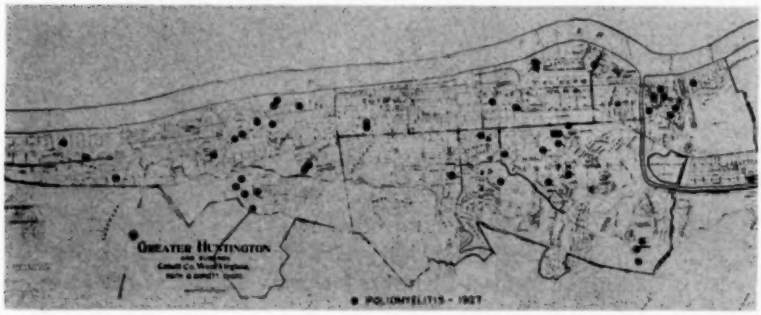

Fig. 4.—Distribution of cases of paralytic poliomyelitis in Huntington, W. Va., 1927.

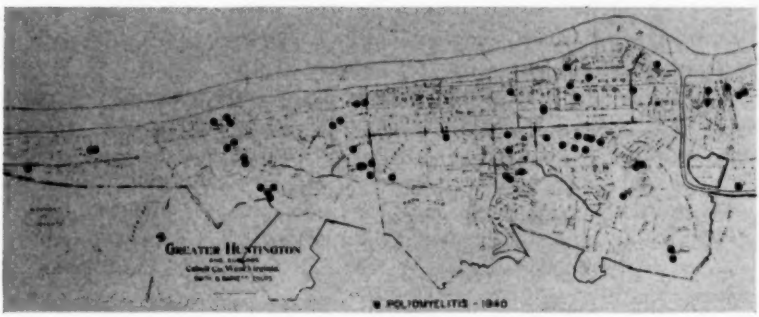

Fig. 5.—Distribution of cases of poliomyelitis in Huntington, W. Va., 1940.

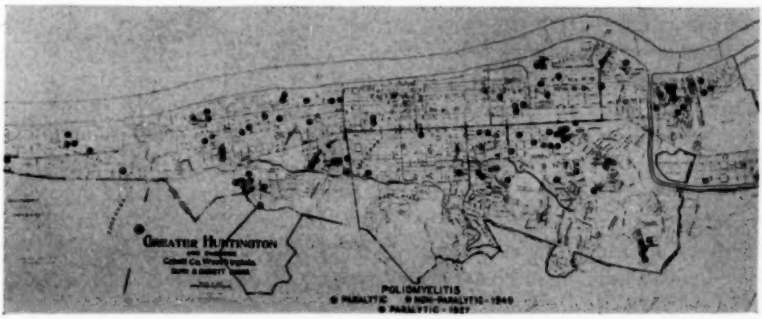

Fig. 6.—Distribution of cases of poliomyelitis in Huntington, W. Va., 1927 and 1940.

Note:

Since the preparation of this manuscript it has been announced that Drs. Trask and Paul of the Yale Medical School have isolated poliomyelitis virus from flies trapped in areas of Huntington which are shown on the spot map as localities where infantile paralysis is prevalent.

EXCESSIVE APPETITE: A BEHAVIOR SYMPTOM IN MALADJUSTED CHILDREN

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LARGE appetite in obese children has been the subject of many discussions, but references to large appetite in nonobese children are rarely found in the medical literature. During a ten-year period at the Emma Pendleton Bradley Home excessive desire for food has been a prominent behavior symptom in maladjusted children. It has appeared as one symptom of poor social adjustment almost as frequently as stealing, lying, physical assault, and other better known behavior symptoms. It was not obvious as a symptom, however, unless certain manifestations were sought in the history.

Hunger is described as an uneasy sensation occasioned by the want of food. Appetite is a conscious longing for something especially desirable. This desire may be activated by hunger, may be the result of training and experience, may be a method of entertainment, or may be an outlet for emotional tension.[4] Large appetite is ordinarily thought to indicate an active, happy, and healthy child. This is true of children who eat heartily after unusual exertion. Persistence of such a longing for food hardly can be considered normal.

Mothers frequently report large appetite as a complaint. A child steals food, steals money with which to buy food, has frequent "snacks" between meals, when awake in the night prowls around for food, and consumes more food at regular meals than both the parents. Large quantities of various types of food are eaten and not specific foods that are liked. One child stole food from the neighbors' porches so often that they asked him in for extra meals. He ate so much that the invitations soon ceased. Another child said that he like to chew his fingers and nails because "they tasted good." A third patient used money which he had earned to buy large quantities of food for poor children. He casually remarked that he had eaten nine plates of beans, with bread and milk, at one meal. On Easter Sunday he ate thirteen hard-boiled eggs, some of which he did not shell. Other children with such appetites worked at small tasks to earn money so that they could buy extra food. One boy associated commonplace events with food; for example, when speaking of a scorched place on his shirt, he immediately associated this with the crisp leg of a chicken and spoke of the amounts of chicken that he could eat. Another made licking motions and noises with his mouth when he mentioned the large quantities of

From the Emma Pendleton Bradley Home.

blueberries or sherbet that he liked to eat. A little girl's excessive appetite became normal after she went away to camp but reverted to its former capacity when she returned home. Another child said that he filed his teeth so that he could chew raw meat more easily.

The usual reaction of a parent to such a symptom is to try to reduce the food intake, without realizing that he is removing a needed source of emotional gratification without supplying something to take its place. The parents fail to recognize that food is merely being used as a support and as a means of overcoming or combating a disturbed mood or psychic frustation.

A sudden increase in appetite is seen occasionally in children subsequent to such situations as the separation of the parents or a death in the family, particularly the death of the parents' favorite sibling.[3] The birth of a sibling or scholastic or social success of a sibling is sometimes followed by a desire for food. The advent of an outsider in the home, or major changes in living arrangements, when facilities for the child are curtailed, may precipitate a longing for food.

Frequently an increase in a child's appetite is favored by the parent. Situations are encountered where the mother's primary manner of expressing affection for a child is in offering food. She uses this ruse to gain the child's affection.[2, 3] The parent occasionally offers large amounts of food to a child who has previously been unwanted. The child, in turn, demands food in combination with other gifts and privileges as assurance that the parenteral means of support will never be recalled.[1]

When the child is a member of a large family or in a position in the family constellation to receive less recognition than his brothers or sisters, there is sometimes a complaint of excessive appetite. This is seen in children from families in which there is a dearth of social contacts and cultural interests. It is also observed where a parent dwells on his or her own unhappy childhood or later illnesses and dissatisfactions and is unable to serve capably as a parent. There is a consequent partial or complete rejection of the child.

The psychoanalytic interpretation of longing for food is that of an intense oral-receptive tendency, the wish to be taken care of and to be loved.[5]

The following reports are of children with excessive appetites who were not obese. The height and weight of the patients were average as compared with standard height and weight tables at the time of admission and discharge. Physical examinations revealed no abnormalities. Blood studies, urinalyses, and blood serology, as well as glucose tolerance tests and basal metabolic rates, were normal. There were no physical changes or changes in weight with the decrease in appetite which followed psychiatric treatment.

CASE REPORTS

PATIENT 1.—John was 9 years of age when he was admitted to the hospital. The complaints at the time of admission were stealing, failure in school, and negativistic behavior. For the first three and one-half years of life John had consumed more food than is normal for the average child. When he was 3½ years of age, his mother left his father to remarry. The mother, an illegitimate child, was mentally dull, exhibited bizarre behavior, and was irresponsible and sexually promiscuous. The patient was cared for after the divorce by a stepmother. He was the third child in a family of five children. One brother and one sister were older, and a half sister and stepbrother were younger. The two whole siblings became involved in stealing and in sex relations with adults. The father was described as affable, indulgent, and financially insecure.

After John was 4 years of age he developed an excessive appetite. He stole milk and bread from neighboring porches and ate everything that he could obtain, including discarded food from garbage containers. He frequently locked himself in the bathroom and caused himself to vomit and returned to ask for more food. Every motive was described as centering around attempts to obtain food. He stole money to buy food and stole small objects, such as pencils and toys, which he exchanged for food. Other hazardous adventures, such as sitting on fires and walking against traffic lights, were described. His school behavior was unacceptable, and he frequently failed in his subjects. His I. Q. on the revised Stanford-Binet test was 89.

John showed improvement as the result of personal interviews that were intended to help him understand his family and economic situation. His craving for food decreased. Community outlets were arranged after discharge.

PATIENT 2.—Bobbie came to our attention when he was 11 years of age. His mother complained of his masturbation, sex play, nocturnal enuresis, and destruction of property when Bobbie was admitted to the hospital. Since the time of the birth of a brother, when Bobbie was 2½ years of age, definite unacceptable behavior patterns had been exhibited. Bobbie was cared for entirely by a nursemaid. Masturbation became a problem, and the child became irritable, destructive, and deliberately voided about the house. Following the discharge of the nursemaid when he was 5 years old, this unacceptable behavior became more marked. Nocturnal enuresis and sex play were pronounced. The large appetite that had been a problem since the birth of his brother increased, and Bobbie consumed more food than either his father or his mother. He sought discarded food from garbage pails and stole food as well as money with which to buy food.

His mother was neurotic. She had many paranoid attitudes and cited three "nervous breakdowns." The mother and father were divorced when Bobbie was 7 years of age. The mother described the child's father as "deceiving, selfish, and brutal," and she considered him insane. She constantly identified the patient with his father.

The patient had one brother, one sister, and one half brother, all of whom were older than he. The death of the sister was attributed to the brutal care of the father when this child had pneumonia.

An I. Q. of 97 was obtained on the revised Stanford-Binet psychometric test.

Personal interviews were designed so that Bobbie might have close contact with one person and might be helped to understand his mother's personality. Bobbie explained that he did not eat so much while in the hospital because he "didn't want to take the food away from the other children." Community outlets arranged for him were curtailed by his mother, who, in spite of psychiatric treatment, continued to identify Bobbie with his father.

PATIENT 3.—Don was admitted to the hospital when he was 11 years of age. Lack of sustained attention, disobedience, overactivity, and destructiveness had been observed since infancy. Nail biting began when Don was 6 years of age. Daydreaming, peculiar grimacing, and frequent failures were complaints from the school. Don stole small amounts of money and food from the home and took carpenter's tools from a neighboring store. He ate excessive amounts "quickly and like a little pig," according to the mother's description. He did such things as "get up at six o'clock in the morning and make himself some French fried potatoes." Don's fantasy life was almost filled with thoughts of food. He spent long periods of time citing the unusual amounts of food that he could eat: twenty-five oranges with the peel and 2 pounds of "84-cents-a-pound round steak." He insisted that his frequent daydreaming was about "something good to eat." He suggested to the children on the ward that he liked to eat magazine covers and did this to prove his statement. He felt that he was losing much weight in the hospital because thick steaks, roasts, and pies were not served daily.

The child's father was a skilled laborer who associated daily with a group of late adolescent boys. He was clever at shooting darts, swimming, wrestling, and boxing. Don's mother, who was older than his father, had been married twice. She cited many illnesses and one "nervous breakdown." She had grandiose ideas about the trips that she was going to take and about her impressive family background. Financial and social circumstances did not warrant such concepts.

Don was the oldest of three children, two boys and one girl. The second child, a boy, was described as "the pet of everyone." A cousin, Don's age, was held up as a model for Don's achievement in school.

An I. Q. of 115 was obtained on the revised Stanford-Binet test.

Don's treatment in the hospital included psychiatric interviews. The purpose of the interviews was to establish a close contact with an adult. He continued to talk at great length about the unusual food and unusual amounts of food that he had consumed but his longing for food diminished.

PATIENT 4.—Ray was 7 years of age when he was brought to us for help. Hyperactive behavior, lying, petty stealing, and masturbation were the complaints. He was an illegitimate child, adopted by his present parents when he was 3 years of age. He had previously lived in institutions and foster homes and had been ill treated and neglected. For three years following adoption Ray frequently cried without cause. He was told of his adoption when he was 5 years of age and later often asked his adoptive parents, "You do love me, don't you?" The parents stated that Ray had an unusual appetite, ate as much as either of the parents, and asked for food between meals. Meals in the home were always prolonged because of the large amounts of food that he seemed to require. The parents described this as an "excellent appetite" and were pleased with it.

The adoptive father, a Swedish cabinet maker, was described by his wife as being affectionate and fond of the child. The adoptive mother was Swedish and excitable and expected model behavior from the patient. She was a meticulous housekeeper and was unduly alarmed when Ray was noisy or untidy about the house.

An I. Q. of 115 was obtained on the revised Stanford-Binet psychometric test.

Psychiatric interviews were started but the child was removed from the hospital against advice after two weeks of treatment.

PATIENT 5.—Jimmie was 7 years of age when his parents brought him for treatment. The mother complained that he had had frequent temper displays since infancy. Following a mastoid operation when he was 5 years of age, Jimmie became more seclusive than previously. He cried at the slightest provocation. He became hyperactive and temper displays increased. His appetite was larger and

the parents frequently forcibly stopped him from eating because he would eat so much that he became ill. He seemed excessively modest and took care to remain covered, stating that he "didn't want to go out bare."

The father, a quick-tempered man, had been in the navy and later worked at odd jobs. He often came home drunk and beat his wife and children. He disliked the noise that the children made. Jimmie's mother had worked before and after marriage in textile mills. She described herself as "nervous." The economic situation had always been marginal.

The patient had an older sister and a younger brother. The sister was hyperactive, attention-seeking, and retarded in school. The brother had convulsive seizures.

An I. Q. of 90 was obtained on the revised Stanford-Binet test.

Jimmie's shy behavior in the hospital appeared to be on a conscious level and was considered a play for attention rather than an indication of a real seclusive nature. His excessive appetite decreased. Treatment was designed to give Jimmie contact with an affectionate adult who saw him in interviews regularly and arranged for attention to be directed toward him.

PATIENT 6.—Arthur came to the hospital when he was 10 years of age. Nocturnal enuresis and hyperactive behavior were the complaints. Arthur was the only child of elderly foster parents. He was adopted from a state institution at 9 months of age. His own mother, unknown to the patient, was a niece of the foster father. She had been a sex problem in her early life and had at least one other illegitimate child besides Arthur. The father was unknown. A maternal aunt was also sexually promiscuous. The patient had never been told that he was an adopted child. The foster father had been economically unsuccessful, and the home was maintained on a government pension.

Arthur was active as an infant and in early childhood appeared hyperactive and attention-seeking. He was irritable with other children and inattentive in school although he was capable of doing good work. Nocturnal enuresis had persisted since infancy. The complaint from the home was that he ate rapidly, filled his mouth with food at each bite, and dropped food all over himself and the floor when eating.

An I. Q. of 123 was obtained on the revised Stanford-Binet test.

While in the hospital, Arthur exhibited behavior similar to that of a 7-year-old child. He associated with younger children, cried easily, and expressed himself with an immature vocabulary. The parents sent him letters and brought him toys suitable for a much younger child. Arthur frequently tried to smuggle food out of the dining room by stuffing his pockets full. He complained that the children discriminated against him when they did not serve him larger helpings of food. Insight into the fact that he was different from the other children was good, but Arthur was not concerned emotionally with any of his difficulties. His appetite decreased with psychiatric treatment, but his emotional maturity remained unchanged.

PATIENT 7.—Gene's mother sought help in the management of her son when he was 7 years of age. The complaints at the time of admission were stealing and lying. Since 5½ years of age Gene had been eating excessive amounts. His mother explained that he "gorged" himself, vomited, and asked for more food. Whenever possible, he stole food from neighbors and from children's lunches at school. There were no particular food preferences, and the mother was unable to account for Gene's appetite.

The mother and father met when the father was in Germany with the American Army of Occupation. Two years after their marriage the wife came to America

to join her husband. The father, a weaver and a cook, at one time deserted his family and was confined in a men's reformatory for this offense. He was brutal toward his wife and children. The mother stated that all of the father's relatives were "queer." The family income was barely sufficient to supply the essentials of life. The patient was the fifth in a family of six children.

Gene showed a great desire for affection while he was in the hospital. He was intensely disappointed when his parents did not visit. Personal interviews were arranged so that Gene would feel that he had an understanding adult on whom he could depend. His behavior improved under this treatment and his appetite became normal.

SUMMARY AND CONCLUSION

A need exists to recognize the emotional origin of excessive craving for food in nonobese and obese children.

This discussion has been written to indicate the occurrence of large appetite as a symptom of maladjustment in children of normal or superior intelligence. The physical and metabolic state of patients seen was normal. Psychiatric treatment resulted in normal appetite with no change in weight or apparent nutrition.

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STUDIES WITH H. PERTUSSIS

VII. Preparation and Assay of Hyperimmune Human Serum

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THE use of human convalescent and immune sera in prophylaxis and treatment of whooping cough has been discussed by Bradford[1] and McGuinness, Stokes, and Mudd.[2] The value in prophylaxis was obvious, but experience in treatment was inadequate for evaluation at that time. More recently, however, human hyperimmune serum has been shown to have value in treatment[3, 4] as well as in prevention. Accordingly, it is pertinent to present information relating to the production and assay of hyperimmune serum.

It is of primary importance, however, to determine which component shall be assayed and which method shall be used before it is possible to determine an optimal procedure for production of serum of highest potency. Agglutinins or antibacterial antibodies are demonstrable in convalescent serum[5, 6] provided that suitable phase I strains of *H. pertussis* are used as test antigen.[7, 8] In the hyperimmune serum, agglutination to high titer is observed.

It has been shown[5] that neither convalescent serum nor hyperimmune human serum contains antitoxin for either the thermolabile toxin (TLT) or the thermostabile toxin (TST) of *H. pertussis*. Indeed, it appears that neither of these toxins is antigenic in human beings, even though they are weakly so in rabbits.[5] Is is possible that even in the absence of demonstrable antigenicity these toxins play an important role in the symptomatology of whooping cough? For the moment this question cannot be answered. It is known that there is a rise in agglutination titer in convalescents from whooping cough. It is also known that following the injection of hyperimmune serum in a child suffering from the disease, there is a rise in the agglutination titer, which rise precedes that which would occur in the natural course of convalescence and is generally accompanied by clinical improvement and frequently a decrease in the total lymphocyte count.[9] Also, according to Bradford and Scherp,[10] while some sera with low agglutination titers give good mouse protection, all sera with high agglutination titers invariably give good mouse protection. This would agree with the repeated observation that convalescent pertussis serum which generally has a low agglutination titer is relatively ineffectual therapeutically.

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Aided by a grant from the United States Public Health Service.

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The observation of Miller[13] that cross protection between pertussis and parapertussis as a result of an attack of either disease is seldom observed and the fact that in rabbits the toxins of pertussis and parapertussis have been shown to be immunologically alike further suggests that the toxins are not an important immunologic factor.

Accordingly it would appear that for the time being, at least, the presence of antibacterial antibodies in high titers gives the best and only simple index of therapeutic value in a serum effective for whooping cough. These antibacterial antibodies would be determined by any suitable bacterial surface-testing means as phagocytosis or agglutination. The latter provides the simplest technical means. Complement fixation may be carried out readily in laboratory diagnosis; it, however, does not distinguish necessarily those antibodies in immune sera which are effective therapeutically unless the test antigen is one of whole organisms that are thoroughly washed free of metabolites and of intracellular components derived from disintegrated or lysed organisms. Purified agglutinogen from phase I organisms would furnish a satisfactory test antigen for complement fixation, but as yet such a test has not been developed.

ASSAY BY USE OF AGGLUTINATION

When a suitable phase I test organism has been obtained, one having satisfactory physical characteristics for agglutination (e.g., not salt-sensitive), as well as proper serologic characteristics, it is advisable to maintain it in a large supply of containers of organisms dried from the frozen state,[10] opening a fresh container monthly. This insures a constant factor in this respect for comparative tests made over a period of years. We have used strain No. 484, a phase I strain which we have shown to have broad agglutinative specificity.[8] After restoration of the strain to a growing culture, three or four culture generations are required to produce an antigen that is not salt-sensitive, but, by using this same procedure each time, a test suspension of satisfactory constancy may be prepared.

For growth of the organisms, standard Bordet-Gengou medium to which proteose peptone has been added, as recommended by Eldering and Kendrick,[11] and 25 per cent horse or sheep blood has been used.

Roux flasks are used for final growth of the antigen. The original dried culture is restored with sterile distilled water and then used to inoculate test tube slants as well as a Petri dish for examination for contaminants. Two further generations on slants followed by inoculation of the flasks provide a satisfactory standard routine procedure. After seventy-two hours of growth on the flasks, gross examination of the colonies and microscopic examination of smears should be made.

The organisms then are harvested by being scraped as nearly aseptically as possible into saline. These are filtered through glass wool and adjusted to a concentration of 2 billion per milliliter by comparison with

an opacity standard. About 200 ml. of antigen of this concentration are ordinarily obtained from a harvest of three Roux flasks. The living organisms are used without addition of preservative. The antigen may be stored up to two weeks under refrigeration at 4 to 8° C.

The serum for assay is then diluted serially in steps of 1:2 in the usual fashion, from say 1:10 to 1:10,240, depending on the stage of immunization. Five-tenths milliliter of each dilution is then incubated one hour at 37° and overnight in the refrigerator with 0.5 ml. of the antigen prepared as described. A supply of a known normal and a known positive serum is kept available for negative and positive controls of the agglutination. These serve as a further check on the uniformity of tests made over a period of time.

A properly shaded fluorescent light is recommended for use in reading, arranged so that the light does not pass directly through the tubes to the eyes of the observer, and thus the observer is unable to see the fluorescent tube itself. The test tube is held against the metal shade, and at times the finger is used to advantage behind the tube in directing the light. In reading, the tubes are tapped lightly against the shade, and where there is true agglutination, the particles, if not already settled, fall to the bottom of the tube. The agglutinate is finely granular. Avoid heavy tapping or vigorous shaking. The last tube in the series which shows some agglutinated particles on the bottom is called a plus one in reaction even though there may be some opalescence in the supernatant liquid due to unagglutinated organisms. In a plus four reaction the supernatant liquid is perfectly clear after light tapping. The last tube in the series in which a plus one reaction is observed corresponds to the titer of the serum. Agglutination falls off rapidly at the titer tube; usually there is but one tube at the end of a series which shows partial agglutination. In negative tubes and in controls, the supernatant fluid is very opalescent; settling, if any, is small in amount, and upon tapping the tubes as described, the settled material is readily dispersed.

PRODUCTION OF SERUM OF HIGH TITER

It has been found that an agglutination titer of 1:1,000 to 1:5,000 is easily attained by immunization in which a suitable vaccine of killed phase I organisms is used, such as commercial Sauer's vaccine. This is over ten times the mean titer found in normal convalescence[6] and would appear to explain the much greater effectiveness of the hyperimmune serum as compared with convalescent serum.

Accordingly, in two selected groups of individuals the effect of immunization by repeated standard series of intramuscular injections was compared with prolonged steady immunization over a period of a year. In both groups, a standard series of a total of 7 c.c. of a suspension of 10^9 organisms given at intervals of seven days over a period of three weeks was used as the first course (1 c.c., 2 c.c., and then 2 c.c. in each

arm). Then in group I this course was repeated every three or four months until three or four standard series of 7 c.c. each had been administered. In group II, the initial series was followed by monthly injections of 2 c.c. of the same suspension. Healthy male adult donors were used in all cases. Test bleedings for assay by agglutination were made biweekly for several months and then about once every month.

TABLE I

AGGLUTINATION TITERS IN HUMAN HYPERIMMUNE SERA

DONOR	GROUP	BEFORE IMMUNIZATION	5 WK.	30 WK.	1 YR.	2 YR.
L. D.	I	0	1,280	2,560	1,280	
H. D.	I	0	1,280	1,280	1,280	
W. K.	I	0	2,560	1,280	1,280	
J. M.	I	0	640	1,280	1,280	
G. M.	I	40	1,280	640	640	
A. R.	I	0	640	640	640	
C. W.	I	0	1,280	160	640	
W. W.	I	0	1,280	320	160	
D. M.	I	0	640	1,280	320	
S. S.	I	20	640	1,280	320	
Average	I		784	1,072	1,100	
A. F.	II	0	320	1,280	640	
C. F.	II	0	10,240	5,120	2,560	
C. M.	II	0	2,560	5,120	1,280	
H. P.	II	0	2,560	2,560	2,560	
J. M.	II	20	2,560	1,280	1,280	
A. S.	II	0	2,560	2,560	640	
L. D.	II	0	5,120	1,280	1,280	
S. M.	II	0	5,120	2,560	2,560	
H. P.	II	320	5,120	2,560	1,280	
S. R.	II	0	2,560	2,560	10,240	
Average	II		3,800	2,688	1,500	
F. B.	II					1,280
A. C.	II					5,120
J. M.	II					2,560
G. C.	II					1,280
P. M.	II					2,560
H. M.	II					1,280
J. T.	II					640
Average	II					2,100

The results of agglutination are summarized in Table I. The difference in the two groups is not significant because of size. The most notable observation is in the variation in titer from donor to donor and even in any given donor from time to time. Some donors are exceedingly refractory from the outset. One donor very early reached a titer of 1:20,000 only to fall subsequently to an average level. The curves showing agglutination titer in a few of the donors (Fig. 1) illustrate graphically the initial rapid rise in titer and the variation which occurs.

Accordingly, in production of serum of high titer an initial standard series of injections is recommended with an assay of the serum by agglutination at the end of one or two weeks following completion of the initial series. Donors' sera whose agglutination titers are not at least as high as 1:1,000 or 1:1,500 should be rejected immediately, since these

donors probably will never produce a serum of high titer. From then on, injections of vaccine should be given at the time of each monthly bleeding of 200 to 400 c.c. of blood. In general, it appears that the procedure followed in immunization of group II is preferable. The titers of the sera obtained at times intermediate between five weeks and one year showed less variation. Furthermore, even after two years, sera from donors immunized steadily by this procedure still exhibited a high titer.

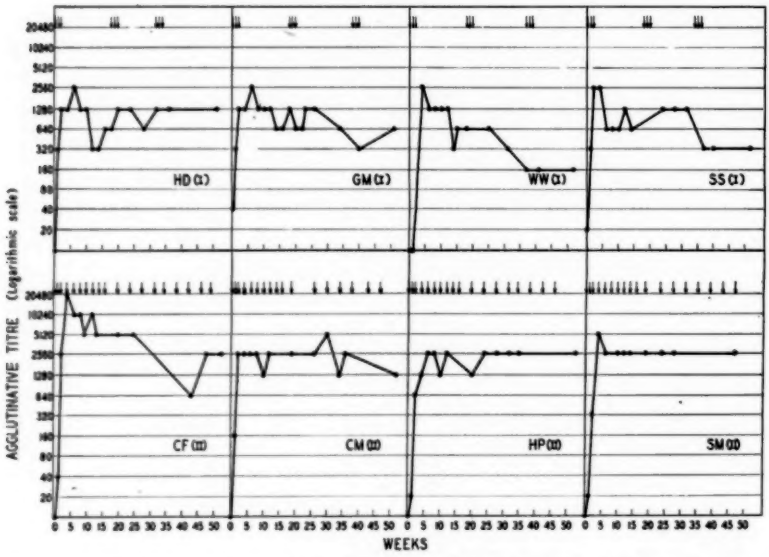

Fig. 1.—Agglutinative response in some individual donors in groups I and II. Arrows indicate times of injection.

In any event, it is most important that the titer of the serum from each donor be determined. Only those sera of high titer should be used. These should be pooled upon completion of appropriate tests for sterility and serologic tests for syphilis as required by regulations of the United States Public Health Service. The titers of sera used in the pool should be such that the final titer of the pool is at least as high as about 1:1,280 or preferably 1:2,560.

SUMMARY

Antitoxin for the two known toxins of *H. pertussis* is not found in human convalescent or hyperimmune human serum. Agglutinins or antibacterial antibodies are found in high titer in the hyperimmune serum of known high clinical potency. Agglutination is recommended as a means of assay of such sera and should be used routinely as a laboratory control test in the production of such sera for clinical use. A procedure for immunization of adult donors is discussed, and the technique

for use of agglutination in such assays is presented in detail. Titers of the sera of a group of human donors during the course of immunization are recorded. Most striking is the variation that occurs in different donors in response to immunization and also in any given donor from time to time. This makes it imperative to follow immunization by laboratory assays of the sera and to use the results as a guide in the selection of donors.

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CONGENITAL TRACHEOESOPHAGEAL FISTULA

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TRACHEOESOPHAGEAL fistula is one of the many interesting congenital anomalies occurring in the newborn infant. Ordinarily it is found associated with cases of congenital atresia of the esophagus but occasionally may occur in infants who show little, if any, esophageal obstruction. In the literature, there is very little reference to this latter type of tracheoesophageal fistula.

Cautley[8] in 1917 found only six cases of tracheoesophageal fistula unassociated with other anomalies and forty-five cases of congenital atresia of the esophagus with a fistula between the esophagus and the trachea or bronchi (88 per cent).

Strong and Cummins[23] in their article published in 1934 state: "In reviewing the literature of congenital atresia of the esophagus, almost every author begins with Sir Morrill Mackenzie's collection of sixty-two instances compiled in 1884 for the report of his own single case. According to Mackenzie, the first reported case was that of Durston in 1670."

Plass[10] in his presentation in 1919 quotes a description of a case observed by Thomas Gibson in 1696.

EMBRYOLOGY

Atresia of the esophagus apparently may appear very early in embryonic life since Plass[10] refers to a specimen in the Harvard Embryological Museum in which the abnormality occurs in a human embryo only 18.1 mm. long; Gruenwald[32] has described the condition occurring in an embryo only 9 mm. long, and Ysander, cited by Rosenthal,[19] in an embryo 8 mm. long.

While there is considerable divergence of opinions regarding the cause of congenital tracheoesophageal communications, it is generally conceded that both trachea and esophagus develop from the same embryonal anlage which consists of an entodermal pouch situated in the thorax behind the heart. About the time when the embryo reaches a length of 4 mm., two lateral indentations or grooves appear on either side of the entodermal sac which become gradually deeper and, when they meet in the center, form the septum, dividing the entodermal sac into an anterior tube which belongs to the respiratory system and the posterior tube which belongs to the alimentary system. The completion of the

Read at the meeting of the American Pediatric Society, May 22-24, 1941, Hot Springs, Va.

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septum takes place first in the caudal end of the pouch and it extends subsequently upward, in cranial direction. When the embryo is 11 mm. in length, the septum formation is completed. Since fistulous communications between trachea and esophagus represent incomplete septal development and since these defects occur close to the caudal end of the sac, such defects may be recognized long before the septal development is completed in the cranial direction.

The location of tracheoesophageal fistulas shows very little variation. In the newborn infant, they are situated at the level of the bifurcation of the trachea or in a distance of ½ cm. above or below that point. Consequently, theories that attribute such lesions to trauma or inflammatory changes in fetal life (Luschka,[19a] Klebs[19b]) seem entirely untenable since any portion of the septum should be equally vulnerable to such forces.

Similar objections could be raised against the theories attributing the lesions to idiopathic septal deviation (Ribbert,[36] Konopacki,[37] and Hoffmann[38]).

Kreuter's[3b] theory claiming that atresias of the esophagus may be explained on the basis that the originally solid esophageal anlage fails to develop a lumen may be entirely disregarded as there is no reason to assume that the entodermal anlage is solid at any stage of embryonal development and this theory would leave unexplained the developmental process of tracheoesophageal fistulas which exist without atresia.

Probably the most plausible theory is the one advanced by Zausch,[13] attributing the lesion to pressure exerted on the primitive entodermal sac by the heart anlage, which acts as a wedge, with the maximum point of pressure directed against one certain anatomical region which coincides with the point where tracheoesophageal fistulas do occur. (According to this concept, if the pressure is exerted on points higher up, it may interfere with the closure of the palatal clefts.)

Rosenthal,[19] however, points out in his excellent review of tracheoesophageal fistulas that there are two valid objections to the acceptance of Zausch's theory, namely: (1) There is no such great proximity between the heart anlage and tracheoesophageal anlage as this theory would suggest since adequate space between the two are clearly demonstrable; (2) should this pressure phenomenon be the prevailing factor, one should expect greater implication of the trachea, which is nearer the point of the wedge, than of the esophagus, and that, of course, is not the case.

TYPES OF ESOPHAGEAL ATRESIA

Vogt[17] has suggested the following classification of the variations of congenital atresia of the esophagus:

1. Complete absence of the esophagus. This type is rare.[12]
2. Cases in which there is an upper and a lower segment, each ending in a blind pouch.

3. Cases with fistulas communicating between the esophageal segments and the trachea or bronchi: (a) With fistula between the upper segment and trachea; (b) with fistula between the lower segment and trachea or bronchus; (c) with fistulas between both the segments and the air passages.

In Lanman's[33] review of thirty-two cases of congenital atresia of the esophagus occurring in the Children's Hospital of Boston, he reports that there were 19 boys and 13 girls, and of these 32 cases, there were 29 cases, or 91 per cent, of type 3 (b); one case of type 2; one case of type 3 (a) and one case of type 3 (c) with some narrowing but not complete obstruction of the esophagus.

A similar preponderance of cases of type 3 (b) is reported by some of the other observers. Thus Mackenzie[1, 2] in a review of 62 cases, reported 40 cases, or 60 per cent, of type 3 (b); Hacker and Lotheissen[16] reviewing 223 cases, reported 173 cases, or 77 per cent; and Rosenthal[19] in reviewing 255 cases, reported 205 cases, or 80 per cent of type 3 (b).

Freudenberger and Kerby[34] have recently reported three cases of congenital atresia of the esophagus with tracheoesophageal fistula, and in one of them, interestingly enough, they were permitted after death to introduce a barium suspension into the upper segment of the esophagus and through an opening in the stomach into the lower segment, and then take an x-ray picture which shows both segments of the esophagus, the stomach, and the tracheoesophageal fistula splendidly portrayed. This case was type 3 (b).

Many authors have written on the subject of congenital atresia of the esophagus (see references) and many cases have been reported, probably 350 cases or more,[35] but unquestionably many cases with and without associated tracheoesophageal fistula have been undiagnosed both during life and at incomplete autopsies, or, as too frequently occurs, because no autopsy is permitted.

Plass[10] states that no two definite cases have been reported in the same family. However, Grieve and McDermott[31] since then have reported congenital atresia of the esophagus with tracheoesophageal fistula occurring in two successive male births in the same family. These children were born in 1937 and 1938 and were both autopsied. The second infant also had an imperforate anus.

SYMPTOMATOLOGY

After seeing a case of congenital atresia of the esophagus with its characteristic symptoms, one should have little difficulty in making a diagnosis, or at least suspecting the presence of the condition in subsequent cases. Because of the accumulation of mucus, saliva, and other secretions in the upper segment of the esophagus which tend to spill over into the throat and from thence into the larynx and up into the nasopharynx, the infant shortly after birth has attacks of choking, coughing, and cyanosis.

He is unable to nurse when put to the breast, and if water or a feeding is given, the liquid is almost immediately regurgitated from the mouth and through the nose with an exacerbation of the above described symptoms. Between these attacks there is an almost continuous drooling of frothy mucus and saliva from the mouth and frothy mucus from the openings of the nostrils.

If a very small catheter is inserted through the nose or the mouth, it soon encounters an obstruction in the esophagus.

If, in addition to the above symptoms and signs, the upper portion of the abdomen occupied by the stomach becomes distended, one should suspect, as suggested by Brennemann[7, 9] that a tracheoesophageal fistula is also present, permitting the entrance of air and secretions into the stomach.

DIAGNOSIS

In the past, the presence of congenital atresia of the esophagus has been confirmed by the injection through a small catheter into the esophagus of a barium suspension, or, more recently, of iodized oil, as contrasting mediums for x-ray diagnosis.

Lanman,[33] however, in his recent article makes the following statement: "Whether or not there is a fistula associated with the atresia, the giving of barium sulfate by mouth is accompanied by great danger and should never be done. Aspiration of barium sulfate alone into the air passages results in an irritative type of pneumonia. Aspiration of iodized poppyseed oil is relatively harmless in itself, but even with the most careful technic there will be some aspiration of the oil plus mucus and saliva containing the oral organisms from the upper segment of the esophagus. It is important also to realize that the use of a contrast medium will not give any helpful diagnostic information that cannot be obtained without its use. Before the plain roentgenogram is taken, a soft rubber catheter should be passed down the esophagus as far as it will go. The level of the upper pouch can be clearly demonstrated by this procedure. If there is no gas in the stomach or bowel, the anomaly is either type 2 or type 3 (a). If the catheter meets an obstruction and there is gas in the stomach or bowel, it is either type 3 (b) or type 3 (c). For practical purposes this is all the differentiation needed preoperatively."

Another practical diagnostic sign is the lack of lanugo hair in the meconium, thus indicating some form of obstruction in the upper portion of the alimentary tract.

TREATMENT

Treatment of the acute symptoms is purely symptomatic, with the use of aspiration and the administration of oxygen, Alpha-lobeline, and perhaps cardiac stimulants, such as coramin, when indicated. Blood transfusions are temporarily helpful, and to combat the dehydration

which soon occurs, intravenous injections of normal saline, or Ringer's or Hartmann's solutions with the addition of glucose should be given.

Feedings to sustain the strength of the infant can be given only per rectum or through a catheter inserted into the stomach after a gastrostomy is done. These measures, especially rectal feeding, are usually poorly tolerated and of no avail in keeping the infant alive very long; in the majority of cases, death occurs during the first week of life. However, Plass,[10] Phelps,[18] Rosenthal and Himmelstein,[21] and Trump[22] report cases where the infant has survived for from fourteen to thirty-seven days.

Surgery in the first few days of life alone offers hope for the ultimate survival of the infant. Many types of operation have been described in the literature, but all, so far, usually have been unsuccessful. The ideal operation apparently should be one in which the upper and lower segments of the esophagus can be joined together and the opening kept patent until healing occurs. At the same time, the tracheoesophageal fistula should be tied off at its tracheal end to prevent the regurgitation of some of the feeding up through the lower segment of the esophagus and the fistula into the trachea, causing an aspiration pneumonia.

If the infant does not die almost immediately or in the first few days of life, death in atresia of the esophagus is usually due to a bronchopneumonia caused by a spilling over of the accumulated secretions in the upper segment of the esophagus into the larynx, thus provoking an aspiration pneumonia.

In the comparatively few cases of tracheoesophageal fistula without esophageal atresia, the treatment in the acute attack again must be symptomatic with the addition of chemotherapy to combat the recurring attacks of bronchopneumonia caused by the regurgitation of some of the feedings into the air passages. Even in these cases, however, it would seem desirable that a successful operation be devised to tie off the tracheoesophageal fistula at its juncture with the trachea to prevent possible regurgitation of the feeding through the fistula.

CASE REPORTS

Colorado General Hospital

CASE 1.—Baby boy S. was admitted to Colorado General Hospital on the service of Dr. L. C. Wollenweber, July 1, 1936, at the age of 3 days because of vomiting of all feedings. X-ray examination with barium was made on July 3 by Dr. E. A. Schmidt who reported complete atresia of the esophagus at the level of the fourth thoracic vertebra. The consulting surgeon, Dr. J. M. Foster, Jr., advised against operation as the condition of the infant would not warrant such radical surgery. The patient died on July 7 at the age of 9 days.

Autopsy performed by Dr. Anderson revealed congenital atresia of the esophagus ending in a blind pouch 8 cm. above the cardiac end. Just below the atresia, which extended 4 mm., there was a communication with the trachea about 2 mm. in size. Death was due to a bilateral bronchopneumonia.

CASE 2.—Baby girl J. was born in Colorado General Hospital on Dec. 19, 1937, and immediately transferrd to the pediatric department, service of Dr. E. Friedman, because of marked respiratory difficulty, excess of mucus in nose and throat, and cyanosis. X-ray examination with barium on Dec. 21 by Dr. E. A. Schmidt revealed "widening of the upper third of the esophagus combined with complete obstruction suggests congenital atresia." The patient died on Dec. 22 at the age of 3 days.

Autopsy by Dr. Benner revealed normal esophagus for about 4 cm., ending in a blind pouch and attached to the lower segment of the esophagus by a cord. There was a tracheoesophageal fistula extending from just above the bifurcation of the trachea to the lower segment of the esophagus. There also was present a congenital atresia of the duodenum and a bronchopneumonia.

CASE 3.—Baby girl B. was admitted to the service of Dr. R. P. Forbes and Dr. R. J. McDonald, Jr., from the obstetrical service on May 13, 1939, the day of birth, because of difficulty in breathing and cyanosis. X-ray examination with barium on May 13, by Dr. McMullen revealed "Apparent atresia of the esophagus ending at the fourth thoracic vertebra. Marked gas accumulation in the gastrointestinal tract." The patient died the same day.

Autopsy by Dr. Boughton: "Upper portion of esophagus ends in a blind pouch 4.5 cm. below the larynx. At this point, there is a fibrous cord attachment to the trachea and also to the lower segment of the esophagus. A tracheoesophageal fistula joins the trachea and the lower segment of the esophagus. There was also an aplasia of the left kidney which weighed 4.62 Gm. Cause of death, bronchopneumonia."

The Children's Hospital

CASE 1.—W. H. F., a male 5 days old, was admitted May 26, 1928, on the service of Dr. G. M. Blickensderfer. His weight at birth was 7 pounds, 2 ounces; weight at the time of admission, 6 pounds, 12 ounces. There was immediate vomiting of all fluids, accompanied by cyanosis; passed meconium but no normal fecal matter; was dehydrated.

Laboratory Report. *Urine:* Albumin +++; acetone, ++. *Blood:* Hemoglobin, 110 (Dare); red blood cells, 7,100,000; white blood cells, 9,800; polymorphonuclears, 54; lymphocytes, 44; large mononuclears, 2 per cent; coagulation time, three minutes.

On May 26 an x-ray examination by Dr. F. B. Stephenson showed inserted catheter and ingested barium both arrested at the level of the fourth dorsal vertebra; no barium in the stomach. Esophagoscopy by Dr. T. E. Carmody on the same day revealed a congenital atresia of the esophagus at the junction of the upper and middle thirds. On May 27 a Wetzel gastrostomy by Dr. G. B. Packard, Jr., revealed small stomach; palpating finger unable to feel lower end of esophagoscope. Patient died on May 28 on the eighth day of life.

Autopsy by Dr. P. Hilkowitz and Dr. C. B. Kingery revealed the upper segment of the esophagus terminated in a blind sac, which measured 6 cm. in length and 1 cm. in diameter. The lower segment of the esophagus, which represented an entirely separate unit from the upper segment, was smaller than usual; the caliber of the lumen was diminished. The consistency of the esophageal wall in the lower segment was firmer than usual, and the upper end of the lower segment entered the trachea just above the bifurcation; several wedge-shaped hemorrhagic infarcts were in the left lung.

Diagnosis was tracheoesophageal fistula, with esophageal atresia and hemorrhagic infarcts of the lung.

CASE 2.—B. J. H., a girl, 3 months old, was admitted Feb. 11, 1934, on the service of Dr. F. P. Gengenbach. Infant was born at the eighth month of pregnancy.

Mother had albuminuria. Birth weight, 5 pounds 8 ounces; weight at the time of admission, 5 pounds, 9 ounces. There was a history of repeated respiratory difficulties with cyanotic attacks since birth. The infant was unable to nurse and regurgitation of all feeding was accompanied by cyanosis.

Laboratory Findings. *Urine:* Negative except trace of albumin. *Blood:* Hemoglobin, 78 (Dare); red blood cells, 3,500,000; white blood cells, 13,000; polymorphonuclears, 42; lymphocytes, 52; large mononuclears, 6 per cent.

An x-ray examination by Dr. K. D. Allen on Feb. 12 is reported as follows: "There is definite intensification of trunk and hilum shadows on the right, suggesting a low-grade type of infectious process or passive congestion resulting from inefficient cardia. No shifting of the heart."

On Feb. 13, while the child was being fed, she suddenly developed marked respiratory difficulty, became very cyanotic, and limp.

An x-ray examination by Dr. K. D. Allen on Feb. 14 is reported as follows: "Ingestion of barium reveals lateral deviation of the esophagus to the left and trachea to the right. Although the barium passes freely into the stomach, some swallows of barium, or portions thereof, enter the trachea above the fourth dorsal vertebra, and it passes into both main stem bronchi and some smaller divisions. The x-ray signs indicate some faulty deglutition mechanism of the epiglottis." After the ingestion of the barium mixture, the patient developed a severe bronchopneumonia and died on Feb. 14 on the fourth day after admission.

On Feb. 16 autopsy was performed by Dr. E. I. Dobos. Exploration of the esophagus disclosed no atresia or any alteration in the contour of the lumen of the esophagus. Upon the opening of the lumen buried in the longitudinal folds of the esophageal mucosa, a very small umbilication was noted. Upon the spreading of the folds of the mucosa, a small fistulous tract appeared, measuring 4 mm. in diameter. This opening is situated on the anterior wall of the esophagus, and, upon the insertion of the probe, it was found to establish communication between the lumen of the esophagus and the lumen of the trachea. The course of this communicating opening is directed upward and anteriorly from the esophagus in an angle of approximately 30°. The opening of the fistula is situated on the posterior wall of the trachea 3 mm. above the bifurcation of the trachea. The lumen of the esophagus was empty. In the lumen of the trachea and in the large bronchi a large amount of milk curds were encountered. Disseminated bronchopneumonic foci were found in the right upper and middle lobes. The heart was greatly enlarged which was due chiefly to the enlargement of the right ventricle. The right ventricular myocardium was greatly hypertrophied; no valvular lesions or any defect in septal development were found. However, there was a wide patent ductus arteriosus. The diminution of the diameter of the aorta in the arch suggested a possible coarctation. On the exploration of the abdominal cavity, no kidney was found on the right side. On the left side there was a very large fused kidney situated just above the level of the promontory, and it presented a very large, disk-shaped organ supplied by two renal arteries, thus indicating that the structure represented fusion of both right and left kidneys. Two separate ureters and pelves were present, the ureters entering the bladder in the usual location.

Diagnosis was tracheoesophageal fistula without atresia of the esophagus, acute bronchopneumonia, patent ductus arteriosus, absence of the right kidney, and fusion of two kidneys on the left side.

CASE 3.—A. M. W., a girl, 4 days old, was admitted Nov. 7, 1935, on the service of Dr. R. P. Forbes. She was not weighed at birth; weight at time of admission, 3 pounds, 14 ounces. Since birth the infant had choked on mucus and became cyanotic every time feeding was attempted.

Laboratory Findings. Urine: Albumin, +++. Blood: Hemoglobin, 100 (Dare); red blood cells, 4,850,000; white blood cells, 10,000; polymorphonuclears, 61; lymphocytes, 37; large mononuclears, 2 per cent; coagulation time, three minutes.

On Nov. 8 an x-ray examination by Dr. J. S. Bouslog showed an obstruction of the esophagus at the level of the second dorsal vertebra. On Nov. 11, 1935, gastrostomy was performed by Dr. G. B. Packard, Jr., and catheter inserted for feeding. Patient died on Nov. 15 on the thirteenth day of life.

Autopsy was performed by Dr. E. I. Dobos and is reported as follows: "There are small bronchopneumonic foci in both lungs. The lower end of the upper segment of the esophagus terminated in a blind sac. The upper segment measures 8 cm. in length. The upper end of the lower segment terminates in the trachea and enters the tracheal wall just above the bifurcation. Upon the examination of the large vessels, a patent ductus arteriosus was found.

Diagnosis was tracheoesophageal fistula, with esophageal atresia, and bronchopneumonia.

CASE 4.—L. J. R., girl, 1 day old, was admitted May 14, 1937, on the service of Dr. E. S. Pratt. Weight, 3 pounds 15 ounces; had had several cyanotic attacks since birth.

Laboratory Report. Urine: Specimen not obtained. Blood: Hemoglobin, 87 (Dare); red blood cells, 4,590,000; white blood cells, 16,600; polymorphonuclears, 70; lymphocytes, 27; large mononuclears, 3 per cent. Coagulation time, three minutes; two nucleated red cells per 100 white blood cells.

On May 15, an x-ray examination by Dr. F. B. Stephenson showed small catheter in esophagus passes to the level of the third dorsal vertebra where it deviates to the right. Barium mixture collected at same level at the end of the catheter. No barium passed into the lower esophagus or into the trachea. On May 16 the patient died on the fourth day of life.

Autopsy was performed by Dr. Dobos: "There is an esophageal atresia, the upper segment of the esophagus terminating in a blind sac measuring 8 cm. in length. The upper end of the lower segment of the esophagus terminates in the posterior wall of the trachea in form of a tracheoesophageal fistula. The diameter of the fistulous tract is 8 mm. No other anomalies were found."

Diagnosis was tracheoesophageal fistula with atresia of the esophagus.

CASE 5.—J. L. E., a 10-month-old white female, was admitted Jan. 27, 1940, on the service of Dr. F. P. Gengenbach with a history of being in St. Joseph's Hospital for seven months following delivery where she had been under the care of Dr. F. Craig Johnson, a former associate. Her color was poor when born; three days after delivery, she began having attacks of cyanosis and coughing when being fed. The chest which would be clear to percussion before feeding became full of râles after feeding. Bronchoscopy and iodized oil injections were carried out by Dr. C. H. Darrow. The oil was seen in the chest by x-rays.

History revealed that this child had had many attacks of pneumonitis. She had done fairly well on a farina formula by gavage and had been able to take feedings from a bottle during last few weeks before admission to the Children's Hospital.

Physical examination at time of admission revealed a moderately ill child, quite irritable, 10 to 12 months of age, and small in stature. There were many rhonchi and moist râles in the chest transmitted bilaterally; no definite localization.

Laboratory Findings. Blood: On admission it showed 73 per cent hemoglobin; red blood cells 4,370,000; white blood cells, 15,200; polymorphonuclears, 35 per cent, lymphocytes, 65 per cent. Urine: Negative except for 1+ acetone. Throat culture showed hemolytic streptococci and staphylococci. On subsequent admissions with upper respiratory infections, the white blood cells ranged up to 29,000.

The child was put on sulfanilamide, which she tolerated well; the concentration on Jan. 30 was 6 mg., and on Feb. 1 was 5 mg. Temperature on admission was 103.4° F. and fell gradually, only to become elevated again on Feb. 1 to 102°; then it fell to normal and remained practically at normal until the time of discharge.

X-rays were taken of the chest on Jan. 31 which were read by Dr. F. B. Stephenson with the following findings: "There is an area of density in the right upper lobe, adjacent to the mediastinum and also some cloudiness around the right hilum, attributable to pneumonitis. The thymus is not unduly large. Since the upper mediastinal shadow and the trachea deviate to the affected side, some partial obstruction of the bronchial system is suspected."

On Feb. 13 the child was discharged, seventeen days after admission.

Final diagnosis was deferred; condition improved.

She was readmitted on Feb. 25 with another upper respiratory infection, discharged April 21 and taken to Children's Memorial Hospital, Chicago, for consultation with Dr. Joseph Brennemann. She had similar respiratory attacks there and later was esophagoscoped and bronchoscoped by Dr. Paul Holinger. His report follows:

"On attempting to introduce an esophagoscope, a blast of air and frothy saliva was expelled into the pharynx from behind the larynx with each cough. Inspection of the larynx revealed the airway patent, but the left cord was thickened and did not move with respiration. It appeared to be fixed in the midline.

"Bronchoscopy: The trachea contained a large quantity of frothy liquid which had the consistency of saliva. After both bronchi were inspected and found to be normal, the trachea was re-examined. The frothy, clear fluid described above appeared to have its origin in a small orifice slightly to the left of the midline, 2 to 3 cm. above the bifurcation of the trachea. This measurement needs verification.

"Re-examination of the esophagus with the infant esophagoscope: An apparent esophageal obstruction was found 19 cm. from the upper teeth. Time did not permit satisfactory examination and identification of pathology at this point."

Readmitted to Children's Hospital May 29; discharged July 20. Readmitted July 22; discharged Sept. 29. Readmitted Oct. 21; discharged Nov. 11. Readmitted Dec. 12; discharged Jan. 8, 1941. Readmitted April 25; discharged May 1. Present age, 2 years; weight, 28 pounds.

CASE 6.—S. L. D., a 7-day-old girl, was admitted Feb. 18, 1940, on the service of Dr. F. P. Gengenbach with a history of vomiting since birth. Infant had been fed by hypodermoclysis since birth. Each feeding attempted by mouth was vomited.

Physical examination revealed a poorly nourished baby with a rather weak cry; skin was dry and icteric in color; fontanels were open; posterior pharynx appeared injected; lungs clear to auscultation and percussion; heart, negative; umbilical cord in good condition; abdomen, negative.

Provisional diagnosis was congenital atresia of esophagus and bronchopneumonia.

Laboratory Findings. Urine: Essentially negative. Blood: On Feb. 18, hemoglobin, 95 per cent; red blood cells, 5,080,000; white blood cells, 10,100; polymorphonuclears, 61 per cent; lymphocytes, 39 per cent; on Feb. 26, hemoglobin, 75 per cent; white blood cells, 10,800; polymorphonuclears, 51 per cent; eosinophiles, 4 per cent; and lymphocytes, 45 per cent.

X-ray Examination, Feb. 18. Esophagus: Barium mixture swallowed by patient remained persistently in a pouchlike dilatation in the esophagus at the level of the bifurcation of the trachea. Over a period of six hours none passed into the stomach. A catheter inserted into the esophagus did not pass beyond that point. Conclusions: Atresia of the esophagus at the level of the fourth thoracic interspace. Examination and report by Dr. F. B. Stephenson.

Feb. 19, Supplementary Report: There was gas present in both the stomach and small intestine.

Feb. 23, Trachea: After instillation of lipiodol into the trachea by Dr. H. I. Laff, films in the horizontal, semierect, and Trendelenberg positions failed to show that any of the lipiodol had entered the esophagus nor was there any in the stomach.

Feb. 24, Supplementary Examination: The anteroposterior view showed persistence of lipiodol in the right upper lobe with occlusion of some of the bronchial branches. Chest 24 hours later. The right upper lobe was cloudy and there was lipiodol in the bronchial branches in that lobe.

This baby was seen in consultation by Dr. G. B. Packard, Jr., who advised against any surgery. Child died March 10 on the twenty-eighth day of life.

Autopsy by Dr. E. I. Dobos whose findings were as follows: "The esophagus ends in a blind pouch. The length of the upper segment of the esophagus is 2 cm. The lumen is considerably dilated and the wall is greatly hypertrophied. The lower segment of the esophagus was explored from the cardiac end, the lumen was found patent, and upon probing the lumen of the esophagus, it was found that the upper end of the lower segment terminates in the posterior wall of the trachea by a fistulous tract which perforates the posterior wall of the trachea in an acute angle, the fistulous tract running upward and anteriorly. There was a small fibrous cord connecting the lower end of the upper segment with the upper end of the lower segment of the esophagus, bringing about a complete atresia of the esophageal lumen. The diameter of the tracheoesophageal fistula is approximately 5 mm."

It is interesting to note that Brennemann[7] in the concluding sentence of his presentation in 1913 said, "While the utter hopelessness of these cases, if untreated, justifies surgical procedures that would otherwise seem too daring; nevertheless the physician who, after making his diagnosis of congenital atresia of the esophagus, decided to let his little patient die undisturbed, as in Case 3 (B's), can amply justify his course."

CASE 7.—J. A. S., a 2½-month-old white female, was admitted Oct. 8, 1940, on the service of Dr. R. P. Forbes. Patient was a full-term normal infant, weighing 8 pounds, 4 ounces at birth. For several days after birth patient took her feedings quite well; thereafter, she began to have choking and cyanotic spells coincidental with each feeding; this persisted until time of admission. She had had some diarrhea and vomiting simultaneous with formula changes. The day before, on routine weekly check-up, the doctor found the patient to have an elevated temperature and patient had some congestion in her lungs. She began to have a cough when she was 3 weeks old and this persisted until admission. Cough more severe during twenty-four hours previous to admission. Up to that time she took feedings quite well.

Physical examination revealed marked purulent discharge from nose. Patient had rapid grunting respiration with suprasternal tug. Inspiration and expiration of equal intensity; many dry râles in right base posteriorly and left apex posteriorly.

Provisional diagnosis was (1) bronchopneumonia, (2) possible tracheoesophageal fistula.

Laboratory Findings. Urine: Within normal limits. Blood: Count on Oct. 9 showed 85 per cent hemoglobin, 4,200,000 red blood cells, 21,400 white blood cells, 21 per cent polymorphonuclears, 76 per cent lymphocytes, and 3 per cent large mononuclears. On Oct. 12 hemoglobin was 75 per cent with 17,100 white blood cells and 28 per cent polymorphonuclears. On Oct. 10 sulfathiazole determination was 4 mg.

X-ray Findings (Oct. 8). Chest: Examination by Dr. J. S. Bouslog showed congestion throughout both lungs and this was more marked on the right, particularly in

the right upper lobe, indicating a bronchopneumonia. On Oct. 11 a picture was made after lipiodol injection into the esophagus by Dr. H. I. Laff. The lipiodol was seen in the left main bronchus and in the trachea. No definite evidence of a fistula.

Admission temperature was 100°; admission weight, 9 pounds, 9 ounces. Patient started on sulfathiazole. Respirations on admission, 104 per minute. During hospital stay the chest did not clear entirely; patient coughed with feedings. The infant was discharged Oct. 15.

She was readmitted Dec. 3 with a similar history and type of infection, treated with sulfathiazole, and discharged Jan. 21.

Subsequently the patient was admitted to the Colorado General Hospital with a similar attack from which she again recovered under the same treatment. Esophagoscopy and bronchoscopy so far have not been permitted. This child is now about 8 months old.

SUMMARY

In this study of 3 cases observed at the Colorado General Hospital and 7 cases observed at the Children's Hospital, 8 cases of congenital tracheoesophageal fistula proved at autopsy, 1 case proved by esophagoscopy and bronchoscopy, and 1 case suspected clinically, but not yet proved, are reported.

Seven of the nine infants with proved cases, or about 80 per cent, had a congenital atresia of the esophagus; the other 3 infants, including the 1 suspected clinically, had little, if any, esophageal obstruction and could take their feedings from a bottle.

The 9 proved cases were Type 3 (b), according to Vogt's classification. Of the 10 cases, only 2 were boys and 8 were girls. Most statistics show about an equal number of each sex.

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SARCOMA OF THE BLADDER IN AN INFANT

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MALIGNANT tumors of the bladder and prostate are of infrequent occurrence during childhood. While the exact sites of origin of these neoplasms frequently can be determined histologically, there may be considerable doubt at times[1] as to whether the primary growth started in the bladder, prostate, or some fascial plane. In a review of 4,903 autopsies carried out at the Babies Hospital previous to 1924 and reported by one of us (H. G. B.),[2] there was no incidence of bladder tumor. Campbell[3] reviews several of the reported series in his discussion of bladder tumors, notably those of Cancetti[4] and Deming.[5] The total number of malignant bladder tumors among children to be found in the literature is not exactly known, but from these reports it would seem to be less than 100. Beer and Hyman[6] make the statement, "In some 500 personal observations no tumor of the bladder was encountered in childhood."

The latest review of the literature on sarcoma of the bladder[7] shows that approximately 200 cases in patients of all ages had been reported in the literature to that time. The authors of this review add three cases, the ages of the patients being 12, 6, and 65 years. The tumor in the first patient, 12 years of age, was thought to be an enlarged prostate, and the bladder growth was not clearly defined on cystoscopic examination. In the second patient, 6 years of age, the mass also was considered to be prostatic in origin. It apparently has been impossible in infants and children to outline definitely and define the limits of such tumors and differentiate them from prostatic enlargements on cystoscopic examination, a suprapubic cystotomy being necessary to make an accurate study of the pathology.

The following case in a very young child is therefore added to the list of reported cases of sarcoma of the bladder.

CASE REPORT

J. W., 9 months of age, was admitted to the Pediatric Service of St. Luke's Hospital on Feb. 15, 1938, the chief complaint being hematuria.

Past History.—He was born on May 17, 1937, weighing 7 pounds, ½ ounce, at birth. He progressed well: sat at 7 months of age and had one tooth at 9 months of age. He can stand at the present time. He was breast fed for two months, and at the age of 3 months cod-liver oil was given (quantity unspecified) and generally was refused. Orange juice, 4 oz. daily, was well taken from 2 months of age. Cereal,

From the Pediatric and Urological Services, St. Luke's Hospital.

vegetable, and egg had been introduced into the diet when the infant was 7 months of age. His disposition was good, and he had had no previous illnesses. He had lost weight, from 20 pounds, 1 ounce, to 17 pounds, 6 ounces, since the beginning of the present illness.

Present Illness.—The date of onset was Feb. 2, 1938. The mother noted some effort during attempts to void. The quantity was small and the frequency increased. Some evident pain was also observed. The infant had had some inflammation about the prepuce, but this improved after several days without change in the symptoms. He was seen by a physician one week before and again four days before admission, at which times his bladder was full, and he was catheterized after various medications and baths had failed to give relief. Pus was found in the urine. He also had a fever. He had been vomiting frequently three to four days before admission and was unable to finish his bottles. Stools were satisfactory. He had had a cough for the past forty-eight hours. He cried considerably and slept very little. He voided every half hour with evident pain, and for twenty-four hours the urine appeared bloody.

Physical Examination.—This revealed a fretful, fairly well developed and nourished boy. Height was 28 inches; head, 17¾ inches; chest, 17 inches; abdomen, 16¾ inches; weight, 17 pounds, 6 ounces. His temperature was 99.8° F.; respirations, 32. The fontanel admitted the tips of two fingers. The occiput was flat. He had eight teeth and average-sized tonsils. There were some moderate Harrison's grooves, and there was flaring of lower costal margins. Small, shotty, cervical, axillary, inguinal, and epitrochlear nodes were discovered. The heart and lungs were normal. The liver was felt one-half inch below the costal margin. The kidneys were not palpable. An umbilical hernia one inch in diameter was present. No abdominal mass was noted upon admission, but the next day a large boggy tumor was observed in the midline below the umbilicus. The testes were in the scrotum. The genitals, perineum, extremities, and central nervous system were normal. A working diagnosis of hematuria, probably traumatic, was made. On February 16 his urine showed a trace of albumin and many red cells. Blood count showed hemoglobin, 60 per cent; red cells, 4,450,000; white blood cells, 15,800; polymorphonuclears, 44; lymphocytes, 50; monocytes, 6; platelets, 262,000. Bleeding time was two and one-half minutes; clotting time, six minutes; and clot retraction, 2 hours.

Hospital Course.—He ran a gradual downhill course. During the first few weeks he was not uncomfortable, although he had continued dribbling of urine and distention of the bladder. A flat x-ray plate of the abdomen on February 16 and another on February 21, taken for possible calculi of the urinary tract, were negative. His blood urea nitrogen on February 23 was 27.8 mg. On February 24, 9 c.c. of diodrast was given intravenously. The x-ray report was as follows: "There was little evidence of function on either side following intravenous administration of an opaque medium; the pelvis and calices are not outlined." He was catheterized daily through February, and various medications, including prostigmine, mandelic acid, and sulfanilamide, were used without any significant improvement in the patient's condition.

A cystoscopic examination was deferred until March 16, when, after two days of comparative improvement, it was carried out. At this time neither kidney was palpable. The bladder was distended. The prostate on rectal examination showed no enlargement. The urethra was dilated with sounds, and an 18 F. cystoscope passed into the bladder. There were six ounces of residual urine; the bladder capacity was normal. A mass was noted at the vesical neck which extended into the urethra and appeared to be more prominent on the left side. This mass gave the appearance of an enlarged prostate. It extended upward into the bladder, especially on the left side, was smooth on the surface and firm in appearance, and its point of origin or attachment could not be detected. The fundus of the bladder appeared

normal as did the right side of the trigone. The ureteral orifices could not be seen. The mass was thought to be either a hypertrophy or a tumor of the prostate. A retention catheter was left in the urethra.

The temperature increased after this examination and for the next few days ranged between 103 and 105° F. He was given urinary antiseptics and improved somewhat. He continued to have pyuria, and hyaline and granular casts were found in the urine. Any further manipulation was deferred because of the reaction following the cystoscopy. A transfusion was given March 24. It was difficult to maintain the urethral catheter in position, and on April 7 an enlarged hard tumor mass was palpable by rectum and moved freely upon palpation of the bladder. A phenosulphonephthalein test showed a 36 and 48 per cent return for two hours. The blood urea was 18.5 mg. The question of irradiating the tumor was discussed at this time. As late as April 14 he was looking well, the indwelling catheter evidently giving him a certain amount of comfort. The urine continued to show pus, red blood cells, and casts. On May 18 the urea nitrogen was 15.7 mg.

A cystoscopy under general anesthesia on April 20 was unsatisfactory. A pyramidal-shaped firm mass was then palpable above the symphysis, which was undoubtedly the bladder distended by a large tumor. This tumor mass was easily palpated with one finger in the rectum and the other hand on the abdomen. A biopsy was taken during the cystoscopy. The following is the report of the pathologist, Dr. Leila K. Knox.

"Specimen consists of a biopsy of bladder tumor, a grayish white, soft pedunculated mass 1 × 5 × 0.7 cm. in diameter. Sections of the tissue show a very small amount of squamous epithelium beneath which there is a soft edematous and vascular mass of neoplasm. This growth is composed of short spindle-shaped cells densely packed together forming a solid mass, while in a few areas edema is noted. The nuclei are somewhat elongated and occasionally triangular. They vary considerably in amount with some very cellular areas where mitotic figures are numerous. The tumor appears to be a primary connective tissue growth and has undoubtedly arisen from the fascial plane between the bladder and rectum. It is probably a highly malignant tumor."

On April 22 the infant was given radiation, 160 roentgen units, and on April 25, 200 roentgen units over the bladder. On April 26 x-ray of the lungs showed no metastases, and the lung fields, heart, and aorta were normal. On April 29 a nodule 1 cm. in diameter was palpable beneath the skin to the right of the midline about 2 cm. below the umbilicus. The patient was in considerable distress, straining constantly. He had edema of the face and a spiking temperature. His hemoglobin was 30 per cent; red blood cells, 2,600,000. On May 14 he appeared very cachectic but was voiding without the catheter. An x-ray of the pelvis showed no metastases in the bones in this region. On May 19 the catheter was replaced, the urine then being thick with pus. A mass 3 × 5 cm. was felt by rectum, somewhat larger on the right than on the left side. The regional nodes were not enlarged. The infant died on May 19.

Pathologic Report [Abstracted].—There are no remarkable lesions of the skin or mucous membranes. On opening the thorax all the viscera are found in their normal anatomic relationships. The pleural cavities are smooth and glistening; the lungs are well expanded and grayish pink in color. On section they are dry and crepitant throughout. The epicardial and endocardial surfaces are smooth and glistening; the valves are intact. The myocardium is reddish brown and shows no gross abnormalities. The aorta is grossly intact. On opening the abdomen the peritoneum is found to be smooth and glistening. The liver weighs 370 Gm. Its surface is smooth; it has a reddish brown homogenous appearance throughout. The gall bladder and extrahepatic ducts and portal vein are intact. The pancreas, spleen, and adrenals appear grossly normal. The right kidney weighs 60 Gm.; the left, 50.

Remnants of fetal lobulation are present in both. The surfaces are pale, reddish brown, and smooth. On section the right shows the calices and pelvis to be enormously dilated and filled with thick greenish pus. The medullary pyramids are almost entirely destroyed, the cortices compressed and distorted. The mucosa lining the pelvis and calices is dull grayish red and granular. The left kidney shows similar widening of its pelvis and calices, though slightly less in degree, and contains no gross pus. The upper portion of both ureters is widened and tortuous, more so on the right than the left. A large papillary tumor moderately firm in consistency with a grayish red edematous surface occupies the lateral portions of the bladder wall, slightly above the trigone, and extends down on the left side through the bladder neck into the urethra. Its base measures approximately 3.5 cm. in width. The prostatic urethra is markedly widened and forms many pouchlike processes, separated by reddened folds of mucosa. The verumontanum is displaced toward the right. Section through the tumor mass shows it to be dull gray, and moderately firm. An area 2 cm. in diameter in the fundus of the bladder shows extensive suppuration and necrosis; elsewhere the bladder wall is thickened, but the mucosa is relatively intact. The entire gastrointestinal tract appears normal.

Anatomic Diagnosis.—Papillary sarcoma of urinary bladder, chronic suppurative cystitis and urethritis, bilateral pyonephrosis, and cachexia.

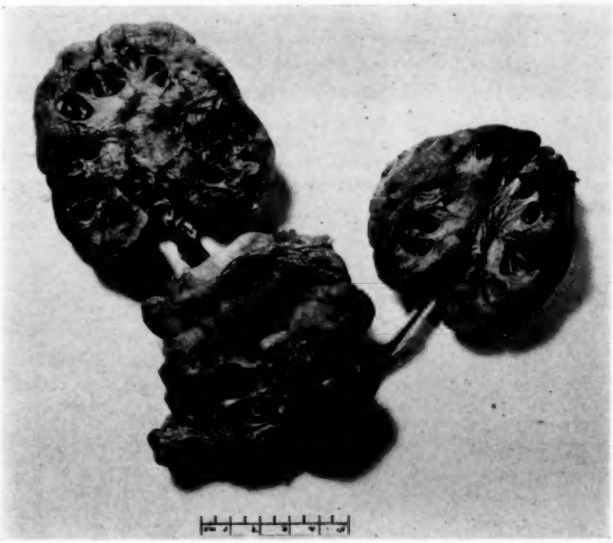

Fig. 1.—Specimen showing bilateral pyonephrosis and papillary tumor on left lateral wall of the bladder.

Microscopic Examination.—Sections through the tumor show the growth to be very extensive, growing out in cauliflower-like masses which are uncovered with epithelium over most of their surfaces. Some of them retain a very thin layer of epithelium, but the entire surface shows considerable infiltration with inflammatory cells. As a whole, the growth consists of dense feltlike masses of fine collagenous fibrils throughout which are scattered small oval nuclei. These are not hyperchromatic; they all contain rather prominent chromatic network, but do not show mitotic figures. Some are hydropic with prominent vacuoles. The blood vessels are only fairly numerous, and tend to have rather thick walls, some of them consisting

of collagenous material similar to that which forms the greater portion of the tumor. The growth extends throughout the bladder wall with only a few hypertrophied muscle fibers remaining. There is considerable infection and atrophy of the prostatic

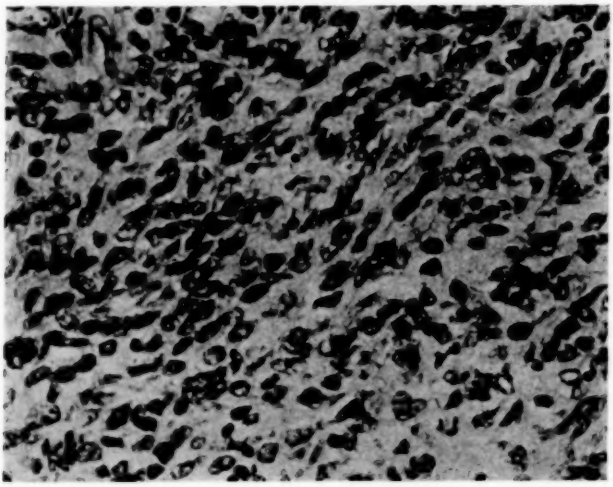

Fig. 2.—High power microscopic section of tumor (×750). (Courtesy of Dr. Francis Carter Wood.)

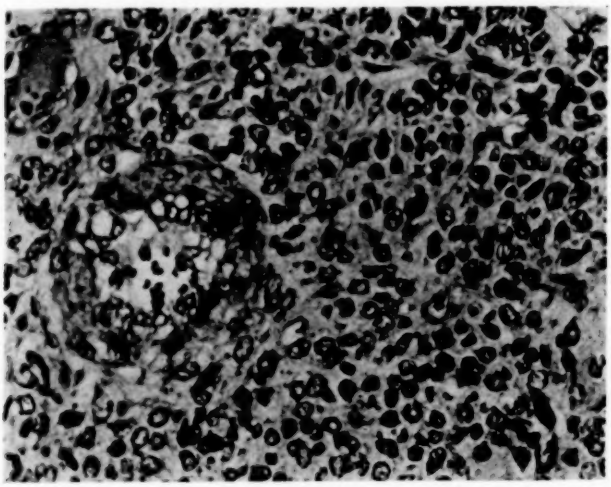

Fig. 3.—High power microscopic section of tumor (×750). The tumor cells appear in the wall of a blood vessel. (Courtesy of Dr. Francis Carter Wood.)

tubules. The exact point of origin of the tumor cannot be stated definitely, but it seems probable it has begun in the mucous membrane of the bladder. The spleen shows congestion and hemorrhage, with much blood pigment. The pancreas is relatively normal. The kidneys show marked infection, the pelvic mucosa being chroni-

cally infected; fibrosis and abscesses are noted in the cortex, and also ascending infection along the tubules which are filled with purulent material. There is much atrophy of the renal parenchyma. The lungs show some atelectasis. The gastrointestinal tract is relatively normal. The adrenals are fairly preserved. The heart muscles show some atrophy. The liver cells also show vacuolization and atrophic changes. The bone marrow is relatively normal. Sections of the brain show edema, but no inflammatory changes. The lymph nodes show no metastases.

Microscopic Diagnosis.—Sarcoma of bladder; chronic suppurative nephritis, bilateral; general cachexia; no metastases.

COMMENT

A review of the literature seems to indicate that sarcoma of the bladder is of rare occurrence. It is found most often in children during the first decade or in adults of the fourth, fifth, and sixth decades. It occurs most often as a single tumor, arising in the bladder wall, frequently in the trigone, and extending into the bladder cavity, rendering a cystoscopic diagnosis of the exact pathology especially difficult in infants, the mass generally giving the appearance of an enlarged prostate. The treatment of these tumors is unsatisfactory, as radical surgery (cystectomy), as a rule, necessitates the transplantation of dilated ureters in the presence of infected, badly damaged kidneys, while less radical procedures such as attempted bladder resection and radiation are invariably followed by early recurrence of the growth, metastases, and death.

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CONGENITAL HYPOPLASTIC ANEMIA

Case Report

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THE following report concerns an infant, now 11 months old, born with an evident anemia, the course of which up to the present is notable in that there has been no tendency toward red blood cell regeneration despite all methods of treatment.

Josephs,[1] in 1936, in a discussion of the anemias of infancy, mentions two cases of an aplastic anemia confined to a failure of erythropoiesis alone, so marked that the infants could be kept living only by means of transfusions administered every four to six weeks. One of these children was so kept alive for eighteen months and the other for five and one-half years, during which time neither child showed any sign of red blood cell regeneration.

Diamond and Blackfan,[2] in 1938, reported a slowly progressive hypoplastic anemia beginning early in infancy, without hemorrhagic tendency, and with the production of an inadequate number of reticulocytes from a bone marrow exhibiting moderate hypoplasia. Four cases are cited, and Dr. Blackfan, in a personal communication, states that he has seen two more since. These authors were able to keep their patients in fairly good health by repeated transfusions at intervals of six to twelve weeks. One child was transfused 113 times, the total amount of blood injected amounting to 26,000 c.c. These children were treated variously with pentnucleotide, iron and copper, iron and cobalt, bone marrow and spleen extract, and vitamin C intravenously, without result; repeated biopsies revealed a hypoplasia of the marrow but not a complete aplasia. In Diamond and Blackfan's experience, transfusions were the only treatment effective in raising the erythrocyte levels, the transfused blood generally maintaining the patient one to two months before gradual wearing out of the injected cells necessitated further transfusion. Despite the recurring anemia, these children continued to grow normally. One patient made a complete spontaneous recovery after two years of treatment. Splenectomy was performed in two cases, with eventual remission and complete recovery in one child a year after operation; there was no response in the other case. The authors feel that failure to transfuse such patients when transfusion is indicated will result in fatal outcome, and that transfusions as necessary will permit normal growth in the hope that spontaneous remission may occur.

Smith[3] states that the sternal bone marrow in a case of this type seen by him revealed a marked reduction in the number of nucleated red blood cells, with an increase of certain primitive cells designated as

hematogones. These primitive cells, present in a ratio of 29 per cent in Smith's case, have been found to be increased in various types of aplastic anemia; they are thought to be primordial forms which probably serve as ancestors for both erythrocytes and granulocytes. The bone marrow also showed an increase of eosinophilic leucocytes.

CASE REPORT

E. S., a female infant, the first child of Polish-Jewish parents, was born June 13, 1940. She was believed to be about two weeks premature. Her birth weight was 2,510 Gm. I examined the infant on the day of birth and noted no unusual findings other than an evident pallor. Blood counts the following day revealed a hemoglobin of 52 per cent with 1,930,000 red blood cells. Slight jaundice was noted on June 15; this disappeared within two days. During the infant's two weeks' postnatal hospital stay, no unusual findings, other than the anemia, were noted. She was given three transfusions of citrated blood, each of 50 to 60 c.c., into the cubital vein during this interval, as well as a 10 per cent solution of iron and ammonium citrate by mouth and ¼ c.c. reticulogen* intramuscularly each day. When discharged on the eleventh postnatal day, the hemoglobin was 73 per cent, and the red cell count was 3,590,000.

The infant's course from this time on can be visualized best from Tables I and II where it will be noted that her blood counts improved after each transfusion only to drop back slowly within a period of several weeks to such a low level that transfusion again became necessary.

On Aug. 1, 1940, at the age of 7 weeks, she was seen in consultation by Dr. Phillip Eckman, hematologist. He found no abnormal cells in the blood smears and considered the condition to be a hypoplastic anemia. Continuation of reticulogen injections was advised and these injections were given thereafter in dosages of 0.5 to 0.75 c.c. intramuscularly every five to seven days. Several intramuscular injections of whole blood were given also, and she received iron ammonium citrate by mouth constantly.

Laboratory studies on Aug. 28 revealed a fragility test in which hemolysis started at 0.38 per cent and was complete at 0.32 per cent, a figure within normal limits. The icterus index on this date was 3.5 units, again a normal figure. The mother's Wassermann reaction was negative during this pregnancy, and the baby's blood also yielded a negative reaction. Stool study for ova and parasites was negative. Repeated reticulocyte counts never gave a yield over 0.5 per cent. At no time were any normoblasts seen in the peripheral blood smear. The white blood count varied from 6,000 to 15,000. Differential counts were not unusual except for an eosinophilia varying from 8 to 14 per cent of the total count; an increase of eosinophiles has been reported in this condition as noted previously. Platelet counts were between 150,000 to 300,000 per cubic millimeter as a rule.

Sternal marrow puncture was performed on November 4 by Dr. Peers Buckley. The marrow was quite cellular, most of the cells being neutrophilic myelocytes with eosinophilic myelocytes more numerous than usual. Megakaryocytes were present in normal numbers. It was the opinion of Dr. J. J. Grabow and Dr. G. Berdez, pathologists, as well as Dr. C. H. Watkins, of the Mayo Clinic, and Dr. Kenneth Blackfan, of Harvard, all of whom examined these bone marrow sections, that, other than for evidence of decreased erythropoietic activity, there was no evidence of an aplastic state.

The child got on very well from a nutritional standpoint in spite of the continued anemia and was given an unusually full diet until the date of her dis-

*Prepared by Eli Lilly and Company.

TABLE I

CHART OF COURSE FROM JUNE 13 TO DECEMBER 23, 1940

DATE	HEMOGLOBIN (%)	RED BLOOD CELLS	WHITE BLOOD CELLS	POLYMORPHONUCLEARS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILES (%)	RETICULOCYTES (%)	PLATELETS	TRANSFUSIONS
6/13 (Date of birth)										
6/14	52	1,930,000	15,100	55	31	4	9			
6/14										50 c.c. (cubital vein)
6/15	68	2,820,000	14,000							
6/18	60	1,810,000	12,400	30	52	5	12			
6/19										50 c.c. (cubital vein)
6/21	71	3,550,000	16,400							
6/25	51	2,000,000	10,000	50	37	5	8			
6/26 (Discharged from hospital)										60 c.c. (cubital vein)
6/29	73	3,590,000	10,000	41	37	11	8	0.1		
7/20	42	1,910,000	6,200							
7/20										75 c.c. (jugular vein)
7/23	50	2,360,000								
7/31	36	1,440,000								
7/31										110 c.c. (jugular vein)
8/ 2	65	3,560,000								
8/26	47	2,610,000								
8/26										100 c.c. (jugular vein)
8/31	74	3,590,000								
10/ 5	34	1,770,000	7,200							
10/ 5										150 c.c. (longitudinal sinus)
10/ 7	60	2,970,000	6,000	40	49	6	14	0.2	338,155	
11/ 4	38	2,220,000								
11/ 5										160 c.c. (longitudinal sinus)
11/ 8	63	3,500,000								
11/26	45	2,350,000								
11/27										180 c.c. (longitudinal sinus)
12/ 2	73	3,970,000								
12/23 (Transferred to University Hospital)										

TABLE II

UNIVERSITY HOSPITAL COURSE

DATE	HEMOGLOBIN (GM.)	RED BLOOD CELLS	WHITE BLOOD CELLS	POLYMORPHONUCLEARS (%)	LYMPHOCYTES (%)	MONOCYTES (%)	EOSINOPHILES (%)	RETICULOCYTES (%)	PLATELETS	TRANSFUSIONS
12/24	6.2	2,220,000	11,200	8	84	4	2	.01	182,000	
1/ 3, 4, 5										Three on three successive days
1/ 6	11.2	4,540,000								
1/ 9, 11, 14										Three bone marrow transfusions of mother's marrow (1 c.c. each)
2/12	6.5									
2/15										Washed red blood cells
2/20	3.6	1,500,000								
2/22, 23,										Several (longitudinal sinus)
2/24	11.6	3.940.000								

charge at the age of 6½ months, at which time she weighed 8,600 Gm., or 19 pounds. Her appearance was quite normal except for pallor; the general accumulation of an unusually firm fat made transfusions increasingly difficult because it obscured the veins. Her last two transfusions while under my care had to be made via the longitudinal sinus because I was unsuccessful elsewhere.

Other than the recurrent fall of the red blood cell count within a period of weeks, with apparent failure of formation of red blood cells as evidenced by inability to obtain a normal reticulocyte increase, there have been no unusual blood findings.

During the age period from 2 to 6 months, the intervals between necessary transfusions varied from three to five weeks, suggesting the fact that the transfused cells were used up during this period and that the patient was unable to manufacture enough of her own cells to keep the erythrocyte count up.

On Dec. 24, 1940, the patient was discharged to the service of Dr. Irvine McQuarrie at the University of Minnesota Hospital. He has kindly submitted the following additional notes as to her course while under his care.

"Physical examination elicited no unusual findings other than that her head appeared rather small, measuring 40.5 centimeters at 6 months of age. The eyes appeared slightly bulging. There were no heart murmurs and the spleen was not, and never has been, definitely palpable.

"Laboratory studies at the University Hospital showed a platelet count of 182,000. Her original reticulocyte count was 0.01%; it never rose over 0.05%. The Haematocrit was 14%, the mean corpuscular haemoglobin 29%, the mean corpuscular volume 70%, the mean corpuscular haemoglobin concentration 41%. The bone marrow erythrocyte volume was 2.7%. The marrow was hyperplastic with regards to the leucocytic series with a lymphocytosis. Normoblasts were very

rare. Urine examinations were negative. Stool examinations showed no gross or microscopic blood. X-ray of the skull and long bones showed no abnormalities.

"The child was given three transfusions of citrated blood on successive days following which her haemoglobin rose from 4.4 grams to 11.2 grams and her red cell count to 4,540,000. On January 9, 1941, January 11, and January 14 she was given a bone marrow transfusion from her mother's bone marrow, about 1 cubic centimeter of the mother's marrow being introduced into the marrow of the baby on each occasion. These procedures had no beneficial result. On February 15, she was given a transfusion of washed red blood cells. Urine bilirubins were determined before and after this procedure. Quantitative tests showed .24 milligrams % in thirty minutes before and 0.65 milligrams % in thirty minutes after. Her haemoglobin continued to fall, however, and on February 20 was 3.6 grams with a red cell count of 1,500,000. Difficulty was encountered in giving transfusions at this stage, and the longitudinal sinus again had to be resorted to. After several transfusions her haemoglobin once more rose to 11.6 grams and the red cells to 3,940,000."

Fig. 1.—Appearance of child at 6 months of age.

CONCLUSION

A case of congenital hypoplastic anemia is reported in which anemia was noted on the first day of life. Study has shown an evident inability on the part of the infant to manufacture sufficient red blood cells to maintain life, so that she is dependent on repeated transfusions for

existence. The failure to produce blood cells seems limited entirely to the erythrocytes; there is no evidence of failure in the production of white blood cells or platelets, so the condition cannot be classed as a true aplastic anemia. The recurrent anemia has not interfered with the ability of the child to maintain its growth and nutrition.

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HISTOPLASMOSIS

Report of a Case in an Infant 15 Months of Age

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CONSIDERABLE interest in the fungous disease, histoplasmosis, described several years ago by Darling,[1-3] has been noted lately because of the number of new cases reported in the past three years. At present it seems to be rare, but it should be considered in any patient with hepatosplenomegaly, enlarged lymph nodes, leucopenia, anemia, cachexia, pyrexia, emaciation, or chronic respiratory infection.

Six cases have been reported in infants under 16 months of age, characterized by emaciation, splenomegaly, leucopenia, anemia, and pyrexia. The first case in an infant was reported in 1934 by Dodd and Tompkins[7] in a 6-month-old infant. Later, in 1939, cases were reported in infants by Agress and Gray,[8] Schaffer, Shaul, and Mitchell,[9] and Amolsch and Wax.[10] In 1941, cases were reported by Rhodes, Conant, and Glesne,[11] and Anderson, Michelson, and Dunn.[12]

CASE REPORT

History.—A 15-month-old colored male infant, whose home was in Jeffersontown, Ky., was admitted to the Louisville City Hospital, Aug. 15, 1940; the mother complained of his loss of weight and high fever. The onset of his illness seemed to date back three months, at which time he had had "pertussis." Apparently he recovered from this in about six weeks. One month prior to admission to the hospital, he began to have a fever and to lose weight rapidly. The weight loss was estimated by the mother to be 9 pounds. According to the mother, the temperature had fluctuated considerably. There had been no vomiting, diarrhea, or convulsions. The child had been very restless since the onset of the illness.

The past history revealed that the patient was delivered by the Louisville City Hospital physicians, and that feeding, development, and habits were normal.

Physical Examination.—The patient was a fairly well-developed and well-nourished colored male infant of 15 months of age, appearing acutely ill. On inspection, the most marked finding was distended abdomen, chiefly in the epigastrium. The skin was hot and dry. The cervical, axillary, and inguinal lymph nodes were palpable but apparently not tender. Both fontanels were closed. There were no mucous membrane lesions. The tonsils were moderately injected. There was no stiffness of the neck. Examination of the lungs revealed dullness in both bases. No râles were heard. The liver was well outlined with a sharp edge three fingers below the costal margin. The spleen, easily felt two fingers below the costal margin, was about the size of a large lemon, was easy to grasp with one's hand, and was freely movable. There was a small easily reducible umbilical hernia. The temperature was 104° F., with respirations of 25 and a heart rate of 135.

Laboratory Findings.—On admission the red blood cell count was 2,460,000, with hemoglobin of less than 7.5 Gm. per 100 c.c. and a white blood cell count of 4,100. The differential smear showed 60 per cent polymorphonuclear leucocytes, 12 per cent

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lymphocytes, and 6 per cent monocytes. There was evidence of many immature cells. Repeated blood counts showed a persistent leucopenia, dropping from 4,100 on admission to 2,900 a few days before death. Hemoglobin was always below 7.5 Gm. The red blood cell count dropped from 2,460,000 on admission to 1,890,000. The tuberculin, Kahn, and Schick tests were all negative. The urine was pale, hazy, and acid; albumin was one plus; sugar, negative. The microscopic examination showed an occasional fine granular cast, 6 to 8 white blood cells, and many bacteria. Culture of the urine revealed *Staphylococcus aureus*. Throat cultures for hemolytic streptococci and diphtheria bacilli, blood cultures, malarial smears, and urobilin were all negative. The icterus index was 12 and bilirubin was 0.2. The chest plate, on admission, showed evidence of past childhood tuberculosis but no recent activity. A chest plate taken just before death was strongly suggestive of bronchial spread of childhood tuberculosis. Skull plates were also negative. Blood smears showed no evidence of leucemia. Fragility test: Control, initial 0.38 per cent; complete, 0.28 per cent; patient, initial 0.28 per cent; never complete in the dilutions prepared.

Course.—The temperature fluctuated from normal to 104° F. in a few hours. The pulse and respiration remained extremely high during the last week of his illness. The patient became very dyspneic during the last week without any further increase in the size of the spleen or liver. The patient's condition continued downhill, and he soon began to refuse food. Fluids given intravenously and transfusions were of no avail. The patient was very restless, irritable, and cried considerably throughout the course of the disease. The only specific therapy attempted was quinine, but this was soon discontinued because of no response. He died Sept 3, 1940.

POST-MORTEM EXAMINATION

The body was that of a light brown, colored, male infant, 75 cm. in length. Lymph nodes around the neck were easily felt beneath the skin. The spleen was felt against the costal margin. A small umbilical hernia was present.

The peritoneal cavity revealed the intestines to be distended with gas, the spleen to be about four times the normal size, and the edge of the liver to be 2 cm. below the right costal margin and 3 cm. below the ensiform cartilage. The spleen weighed 85 Gm. and was dark purple in color, with a distended capsule. The liver had a slightly distended, clear, transparent capsule. Beneath this was yellow, taffy-colored liver tissue. The cut surface was soft and pale. The kidneys showed fetal lobulations but otherwise were not remarkable. Along the lesser curvature of the stomach and the lesser omentum were many lymph nodes that were hard and shotty and which measured approximately 0.5 cm. in diameter. In the mesentery of the small intestine were many large lymph nodes, the largest being 3.5 cm. in length. These were also hard and firm. The mucosal lining of the small intestine showed hyperplasia of the Peyer's patches with some mucosal ulceration. Along the mesenteric attachment of the large bowel were more small, firm, shotty nodes. These were also found around the aorta. The cut surface of the lungs revealed white, granulomatous areas approximately 2 mm. in diameter. These contained thick, creamy exudate. At the root of both lungs, there were many enlarged glands.

MICROSCOPY

Sections through the granulomatous areas of the lungs (Fig. 1) showed caseation necrosis. Many phagocytic mononuclear cells were seen which contained parasites. These were indentical with those described by Darling and given the name of *Histoplasma capsulatum*. The spleen showed numerous areas of caseation, surrounded by parasitic infested mononuclear cells. The abdominal lymph nodes (Fig. 2) had many small areas of caseation necrosis with parasites in many of the phagocytic

mononuclear cells. The liver showed essentially the same picture. The bone marrow (sections through vertebral bodies) showed the most severe reaction of all tissues. There was considerable reticuloendothelial hyperplasia. Mononuclear, plasma, and occasional giant cells were noted. These were invaded by parasites.

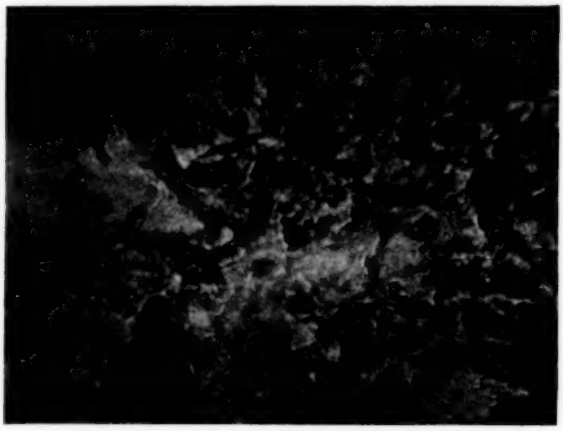

Fig. 1.—Section of lung (×900) showing *Histoplasma capsulatum*.

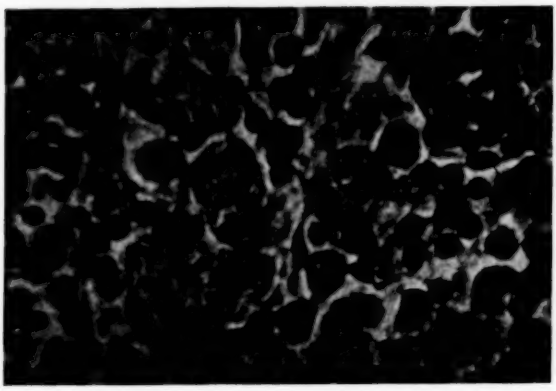

Fig. 2.—Section of lymph node (×900) showing *Histoplasma capsulatum*.

DISCUSSION

Histoplasmosis can no longer be considered a rarity and must be ruled out in any case presenting pyrexia, leucopenia, splenomegaly, hepatomegaly, cachexia, or anemia. Even with varied clinical manifestations the ante-mortem diagnosis can be made from a number of sources.

As yet, there has been no successful therapy, although the following have been tried: x-ray, sulfanilamide, potassium iodide, and antimony preparations.

SUMMARY

A case of histoplasmosis has been reported in a colored male infant, 15 months of age, which is believed to be the seventh case in an infant and to be the second case of histoplasmosis in Kentucky,[15] both patients having been in the Louisville City Hospital within a period of two years.

The author wishes to express his appreciation to the Department of Pathology, University of Louisville School of Medicine, for cooperation in presenting this paper, to Dr. J. A. Kennedy, of the Department of Bacteriology, for his aid in the preparation of this paper, and to Dr. W. F. Manly for the photography.

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THE PEDIATRICIAN AND THE TEACHER

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IT WOULD probably be more or less futile and perhaps presumptuous for me to report any educational research which would make any very significant contribution to your thinking about either the problems of education or problems that are essentially medical. It seems to me, however, that the thing that I might do that would be of greatest help to you would be to indicate some of the ways in which I think medical people and educators might work together in areas in which they have a common interest. I can do that best, not by telling you about your faults and shortcomings (a subject on which I certainly am not competent to speak) but perhaps by telling you about the faults and shortcomings of teachers in schools, because I believe that if you, as pediatricians and medical workers, understood exactly how many difficulties schools and teachers face and just what our weaknesses are, perhaps you could fit your strength and contribution into that picture more effectively than you otherwise would.

I think I need not tell pediatricians about the enormous amount of maladjustment that is brought about by the wrong kind of educational practice and the failure of the school to meet the needs of individual children. You as medical men have from time immemorial thought of your practice in individual terms. The very phrase "adjustment of the child to school" sounds bad to you. You would much rather have us talk of the adjustment of the school to the child. It does not sound any better to you to talk about the adjustment of the child to the school than it would for me to talk about the adjustment of the patient to the hospital, an idea which to you would, of course, seem an utter monstrosity. Nevertheless educators have thought so long in terms of practice which emphasized subjects to be learned and programs to be followed rather than personalities to be developed that we have an extremely difficult battle within the profession to get teachers and schools to see that schools are for children, and we have a very hard time within the teaching profession to get teachers to see that boys and girls are worth more than books. Ordinarily their assumption is that books are more important than boys and girls.

In medicine you have so long stressed individual diagnosis that you have become more sensitive to the needs of individual personalities than teachers have. As doctors, and especially as obstetricians and pediatricians, you have one great advantage over us. You make your entry into the life of the child so much earlier. The average child enters school at the age of six and by that time so much conditioning has taken

Presented at the meeting of Region III of the American Academy of Pediatrics, Chicago, May, 1941.

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place that we have a very difficult time achieving results. Obstetricians and pediatricians enter the life of the child either very soon after birth or in the early stages of pregnancy. It may even be that you are called into consultation on matters of family planning and family relationships even before conception. The importance of personality growth and development in the educational life of the child does not need to be stressed here, but we should think together about some of the research which is coming out of the child development centers and which is throwing light on the kind of climate which is necessary for maximum growth and development on the part of children.

We find, for example, that children who are brought up in an orphanage make slower intellectual and emotional adjustment than children who are brought up in an individual home. We find that affection, security, and freedom are the influences which are most effective in promoting the growth of children intellectually, emotionally, and in all-around personality development. Now if that is true, is it not perfectly clear that the emotional factors, the social adjustment factors, in short, the human relationships which operate in this climate for the growth of the child, are of the greatest importance? Is it not likely that the child's parents have, either for good or for ill, made certain adjustments to one another, perhaps long before the child enters the school, and that out of those adjustments, good or bad as they may be, certain personality conditioning has already taken place? In other words, when we teachers get the child it is often too late to do anything, or at least much harm has already resulted.

Not only do medical men and women come into the scene years earlier, but the parents are much more likely to listen to you than they are to us. You have achieved for yourselves throughout decades a certain professional regard. I do not know whether I should say here that this may in part be due to the fact that the parent has to pay for your advice and that he gets ours for nothing. We will not debate that, but in any case I think that your influence is more effective. It is more effective perhaps for another reason. The coming of a child into a family is an event of great emotional significance in the relationship of husband and wife, and the coming of the child is a great center of interest; when you talk to parents at that period you are in a very strategic position.

All of which leads up to a point of view that I have held for a long time. I believe that the practice of medicine is essentially an educational job, and I believe that every doctor is an educator in the true sense of the word, and I think he should have equipment to be an educator.

Let us leave the medical scene for a moment to look back at the teaching profession. Within the teaching profession we have stressed subject-matter learning. More than that, we have stressed mass learning, and we have carried on our enterprise on a mass basis. Now the few

examples of progressive schools that study their children individually and carry forward their educational programs on the basis of diagnostic procedure are exceptions perhaps that prove the rule. Moreover within the teaching profession, we have more or less ignored the emotional development of the child, and we have not concerned ourselves with total personality development nearly as much as we should. Now notice what happens in the life of a child. For the vast majority of American children the services of pediatricians are not available, so that the service which you people could render with such salutary results just is not available to millions of children. We as teachers and school people have neither the equipment, the knowledge, nor the skill, nor the point of view to do that job as we should, and moreover we enter the scene about six years too late to do our most important job.

Now, putting all of these things together, I believe that teachers should have far greater knowledge of the human organism, of the emotional elements in personality; in short, teachers should know a great deal of what you know. They do not want to take your jobs away from you, but they should know something of what you know about human beings so they can be more sensitive to the factors which enter into a satisfactory climate for human growth and development in the school. Then I think, if you do not already know it, you should know some of what teachers know, so that you can take advantage of influencing the first six years of the child's life. You will influence older children also, but I am thinking particularly of that period when we have no chance at the parents or the children.

The research which has been done in medicine and in education points in the same direction. It indicates that total personality should be our main concern, educationally speaking and medically speaking. Isolated medical treatment, if I read some of your literature correctly, is not viewed as being very acceptable, nor is isolated learning of subject matter apart from personality development viewed as acceptable practice in modern education. Both you and we need to be concerned with the broader aspects of personality development. We are both interested in the development of a climate for creative living on the part of all human beings.

Now let us examine the school to see how our cooperative endeavor is actually going on. Many schools in this country have no school physicians. Many schools have few teachers who are really familiar with the nature of the human organism, its growth and development or its behavior. Millions of American children are going to school in places where there is really no person who is competent to advise on problems of maladjustment or who is competent to arrange an environment which is desirable for maximum growth and development of individual children. Even where there are school physicians I wonder if we are using those school physicians in the best way. Is it not true that a great

deal of the effort which these people can put forth has to do with the control of contagious disease, with the correction of physical defects, the removal of tonsils, and so on, and that very little of the school physician's effort goes into the problems of emotional and personality adjustment?

Have we trained school physicians in the best way? Is it possible that physicians generally, because of the nature of medical practice, have found it necessary to emphasize the pathologic and abnormal rather than the normal, and that the average school physician is better equipped to take care of physical defects and to deal with the control of health generally in a social way than he is to deal with the problems of personality adjustment on the part of individual children? Now if that is true, then perhaps we need modifications not only in the training of teachers, but also in the training of those who are to serve as school physicians. In fact, I wonder whether it is not going to be incumbent upon us to merge in some measure the activities of these two groups of people. If I could influence the work of these two professions I would bring them much closer together than they are at the present time. There should be teachers here listening to these programs. The previous speaker said some things that might well have been heard by every teacher in Chicago. Every teacher in Chicago should have heard the comments which the previous speaker made on the question of sex education alone, but it is not only the matter of our hearing what should be done; we should know something about the scientific basis for the things that we ought to do, and I am glad personally that I came in early enough to hear some earlier parts of this paper which were used by the speaker as a basis for the advice which he later gave to teachers, and if I may be presumptuous enough, I should like to suggest that I think there are things going on in educational circles which would be worth while for you people to hear.

Maybe we should have joint meetings of pediatricians and physicians and teachers where we could concern ourselves with the problems of human growth and development, of child development, of education. Education is one of our oldest professions and it is one which intrudes itself upon the life of everyone and yet it is one that is most misunderstood. When we attend parent-teacher meetings the questions which laymen bring to us are a simultaneous evidence of the interest of the layman in educational problems and of his lack of understanding. You have that problem, too, but I think so far you have probably done a little better job of familiarizing the layman with your profession than we have. I think we both, however, have the job of helping parents and people generally to a better understanding of the problems of child care and development and education.

May I illustrate? The biologist tells us that every human organism is unique. For example, of all the people in this room no

two of you are alike. More than that, if I take any one of you there has never been a person like you in the world before and there is never going to be one again. Every child that enters your practice presents a unique problem that neither you nor any other pediatrician has ever faced before or will ever face again after that child has made his exit from the world. Every human being is a unique phenomenon. He possesses creative powers which no other human being possesses. If he becomes a painter he will paint a picture that nobody else could paint. If he is a musical composer he will write a symphony that nobody else could write. No matter what his endeavor may be, he is a unique personality. The problem of education, you see, is the problem of giving each of these unique personalities the opportunity to develop as a unique personality and to make that contribution to society as a whole which that personality alone can make.

Now it is the glory of the democratic way of life that it alone of all the social patterns holds out to individual human beings the right to be themselves and the right to be unique personalities. You may not have thought of it but when you as a physician or as a pediatrician go into a home and help the parents to create for an individual child a really favorable climate for the growth and development of that child as a unique personality, you are practicing democracy in one of the real ways in which it can be practiced as opposed to totalitarianism. If we believe in totalitarianism we would take that child and shape him for whatever purposes we had in mind and ignore his unique personality characteristics. I do not, therefore, see how you people can ever be converted to totalitarianism no matter what happens to the rest of us, because I believe that everything in your medical science is in conflict from a social and a philosophical point of view with the totalitarian concept of life.

I mention that because I should like to leave with you the idea that there is a relationship between education and social patterns of various kinds. There is a relationship between science and social patterns of various kinds. When we are practicing these professions of education and medicine, we are working out the principles of our way of life. Our way of life has an impact upon our profession and the spirit in which we conduct it, and I think that you, as members of the medical profession, and we, as members of the teaching profession, have a joint responsibility to create in schools and in homes and in communities the kind of environment which will help individual children to make the most of their capacities and in turn to make the greatest contribution to the social structure as a whole. That is democracy, that is good teaching, and, with your permission, that is good practice of medicine.

THE TRAINING OF THE SCHOOL PHYSICIAN

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EDUCATION, by definition, sets about systematically to instruct individuals in preparation for the work of life. There is striving for an educational ideal and goal. As the medical historian Sigerist[1] has pointed out, the educational ideal of general education is the ideal citizen; of medical education it is the ideal physician. These ideals are related one to the other, the first defining the role of the second and both being influenced by social and economic factors in society. The demands of society for changes in education seem especially harsh in times of great transition such as we are experiencing now, and educators are reluctant to change until cautious investigation shows that change is warranted. Progress seems to be by fits and starts and by periods rather than by gradual evolution. Medical educators have been less inclined to experiment in medical education than in medical science and, like other technical instructors, have taken courage to do so only after successful experimentation in general education has demonstrated the need for concomitant changes in the special fields. Of necessity, then, there is a lag (physiologic rather than pathologic) in the changes of medical education, but once stimulated, response is usually profound.

Primary and secondary schools, in preparing the ideal citizen for life, have long realized the importance of good physical health in the learning process. This stimulated the creation of the school doctor, a part-time physician interested in the sick child, a physician who often took the school position as a partial means of livelihood until his private practice became suitably remunerative. Society, however, was not content that the physician be interested primarily in overt disease and demanded attention to states of potential illness as well. The school physician became interested in prophylactic measures against communicable disease, in conservation of vision and hearing, and in the effects of tonsils and adenoids and carious teeth on health. And next came the realization that all disease was not physical but might be mental, and that physical illnesses usually had some psychologic accompaniments. Progressive educators in general education, realizing increasingly the role of preventive medicine and the place of mental hygiene as well as physical hygiene in pupil and teacher alike, sought guidance from the school physician in the interpretation of behavior and in the better understand-

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Presented before the School Health Section of the Institute on Personality Development of the Progressive Education Association, April, 1941.

ing of educational problems and even in the modification of curricula and teaching methods. The medical adviser should now be a highly specialized individual, incorporating several disciplines in his training and in his medical functioning.

In examining the present-day preparation of the school physician, one finds inadequacies in several spheres; some are primarily inherent in present-day medical education in spite of its great scientific and technical advances and appear, for example, in the lack of coordination of the medical specialties, the relative isolation of preventive medicine from the practice of medicine, and the neglect of emotional, social, and economic factors in consideration of disease states. Other deficiencies are primarily inherent in the general education system. The school physician of today, in spite of his increased obligations to the school, is still relatively uneducated as far as the first part of his title is concerned. The very duality of the term "school doctor" should suggest the need for training in "school affairs" as well as medical matters. The weaknesses demonstrated in this area are due in part to the educators' unwillingness to share their problems with the medical groups, and in greater part to the unwillingness of the latter to share in the consideration of what seemed to them to be "nonmedical" affairs. The training of school medical personnel must be a joint enterprise of medicine and general education. It cannot be achieved by adding a few courses to the already top-heavy medical school curricula of the immature undergraduate student. It should be a learn-by-doing process and may be approached best through postgraduate instruction with the graduate physician who has reached the maturity of his own psychologic development and of his medical thinking which fosters an interest in matters of health as well as of disease, and for whom the career in school medicine is as stimulating as bedside practice or the dramatic glamor of operating room and post-mortem table.

The proposed preparation period may be divided into two parts: the first in basic pediatrics in the medical clinics; the second in general and special education in suitable training schools. In considering the first of these, it is important that the pediatric training include (1) a one-year hospital service on the inpatient service of a children's ward to allow twenty-four-hour observation, study, and care of sick and convalescent infants and children, with emphasis, however, not only on organ pathology and disease entities, but also on consideration of the total individual in the changing hospital setting; and (2) a year in the outpatient clinics to permit care and study of ambulant patients and of the well infants and children in the different settings of family, community agency, foster home, and school. Modern pediatrics is focusing increasing attention on the mental, emotional, and social development as well as on the physical development of the child, and the pediatrician-in-training is able to understand the complete person only when aided

by parents, private physicians, and the auxiliary medical personnel of school administrators, teachers, child guidance workers, dentists, nurses, social workers, and court officers. The doctor in the outpatient service must have time for frequent case conferences with these persons and for case supervision by psychiatrists and pediatricians with special training in psychiatry in order to develop a better understanding of the psychologic problems of children from nursery school age through adolescence and of psychopathologic factors in parents which influence the life of the child. Well-trained social service workers will help the physician follow the progress of each individual by skillfully steering the child through the various medical and social units.

In considering the special training in the general educational centers which would come in the third, and possibly a fourth, postgraduate year, time would be spent in primary, secondary, and special school internships under the direction and financial support of the school and municipal health departments. The trainee would have an adequately supervised, full-time, rotating service in the schools in order to familiarize himself with its daily life, its physical structure, and personnel; he should not be set off from the rest of the school workers but should move about the premises, visit classrooms, and be available to students and faculty. The physician would make examinations of healthy and sick children, appraise physical and mental health, have time to interpret these results in simple, nontechnical language to teachers in group faculty meetings or in individual interviews, and consider the needs of the "average normal" and the "handicapped" pupils with parents, school personnel, and private and clinic physicians with whom the responsibility for adequate medical therapy would continue to rest. In cases where parents or children prefer that routine physical examinations be carried out by private practitioners, methods for exchange of the results of the examinations between examiner and school physician should be worked out. Time for recording human conduct and for research in child development should be included in the work schedule. Regular conferences with well-trained and competent superiors are necessary, since the aim of the teaching process is not only to give the student an adequate body of knowledge, but also to provide supervised experience.

Having finished the three- or four-year course, the newly trained physician should find ready a suitably remunerative part- or full-time position which would offer him opportunity to carry on the work of his learning period and allow him to instruct other trainees and to keep abreast of new developments in his field through periodic conferences with colleagues and supervisors. The continued education of physicians already engaged in school work should be an essential part of the program. For these physicians and for the teaching groups working with them there should be organized short courses. The Institute

on Personality Development of the Progressive Education Association, through its seminars and summer workshops, has already established such training for mixed groups with common problems as well as for single professions with special interests. This venture, so successful in the general education milieu, could benefit and contribute much more if a closer working relationship were brought about with departments of pediatrics and psychiatry in medical schools and with municipal departments of health. Separation of these disciplines, which is important for each in the initial phase of its development and which must continue in part for the advancement of special techniques, should not constitute isolation. Each will grow in a healthy manner only when segregation is broken down, complementary ideas are integrated, and common purposes achieved.

Disease and health, whether public or private, curative or preventive, are no longer matters of concern to single departments in a medical school, whether it be a department of public health, pediatrics, psychiatry, or even surgery, nor to single aggregates of lay people, whether they be in the religious, educational, or legal fields. The successful training of school physicians is the responsibility of many: the trainee, the medical and general educators, and the citizens in the community who provide money and create professional opportunities.

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American Academy of Pediatrics

Proceedings

TENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

MEMPHIS, TENN.—NOV. 18-20, 1940

Round Table Discussion on Chemotherapy

Chairman: John A. Toomey, M.D., Cleveland, Ohio
Associates: Alexis F. Hartmann, M.D., St. Louis, Mo.
John A. Bigler, M.D., Highland Park, Ill.
Henry F. Helmholz, M.D., Rochester, Minn.
Edward B. Shaw, M.D., San Francisco, Calif.
Edwin E. Osgood, M.D., Portland, Ore.
Secretary: Ernest S. Watson, M.D., Elmhurst, Ill.

Background of Chemotherapy

John A. Bigler, M.D., Highland Park, Ill.

Chemotherapy is almost as old as the art of medicine. There has been a continuous search for specific drugs and remedies which could be used in the treatment of disease. In spite of the many years that this search had been going on, up to modern times only three remedies worthy of being called specifics had been discovered. One of these was mercury, a metal used in the treatment of syphilis, and two were vegetable preparations, cinchona bark (quinine) for malaria and ipecacuanha for certain types of dysentery. No further noteworthy advances in chemotherapy were made until the development of bacteriology and advances in chemistry.

Modern chemotherapy dates from Ehrlich, and he can rightly be called the father of chemotherapy. Ehrlich tried many synthetic dyes in animals with trypanosome infections with some degree of success. With Shiga in 1904 he developed a benzedrine dye, trypan red, which was trypanocidal. A few years later Mesnil and Nicolle developed a toluidine dye called trypan blue which was effective in a protozoal infection of dogs and cattle. They also developed another dye called trypan violet which was the forerunner of a more complex sulfonic acid preparation used in the treatment of trypanosomiasis. About this time a dye called scarlet red was prepared which is still used in the treatment of chronic ulcers.

During this period the parasite of syphilis, a spirochete, was discovered, and Ehrlich began his epochal work with the arsenicals, developing in 1910 salvarsan, his six hundred and sixth preparation, a specific for the disease of syphilis. This was the greatest discovery in chemotherapy in modern times and is equalled only by our most recent chemotherapeutic agent, sulfanilamide.

Ehrlich also found that a yellow acridine dye, trypan flavine, had some beneficial effect on the trypanosome which causes African sleeping sickness.

More recently, Young, White, and Schwartz combined mercury with a fluorescein dye. This preparation known as mercurochrome 220 is now used as an antiseptic, but it has not lived up to its expectations for internal use. Another dye, gentian violet, developed by Churchmann, is now used externally for bacterial and fungus infections.

Morganroth and Levy in 1911 found that ethylhydrocupreine (optochine), a derivative of quinine, was an effective chemotherapeutic preparation in the treatment of pneumonia in mice, but this preparation has not been so successful in man because of its toxicity when used in the required effective dosage.

This covers the most important phases of chemotherapy up to a few years ago. There was some success in the therapy of protozoal and metazoal infections, but in so far as bacterial infections were concerned, only successful antiseptics were developed. Only in 1935 was it discovered that the sulfamido dyes might prove effective in the treatment of infections caused by the common bacterial invaders which, incidentally, are the cause of most diseases of man. It seems only right that the development and the discovery of the sulfonamide preparations should be so intimately related to the synthetic dyes with which Ehrlich worked for so long.

Oddly enough, sulfanilamide was chemically prepared by Gelmo in 1908 while Ehrlich was in the midst of his work with synthetic dyes. No thought was given as to its chemotherapeutic activity. Chemists in the dye industry were working with azo dyes which contained sulfonamide groups. Commercially these dyes were found more satisfactory than the azo dyes which did not contain the sulfonamide groups. No attempt was made to study the action of these dyes on bacteria until 1935 when Domagk, using two azo sulfonamide red dyes developed by Mietzsch and Klarer for the dye industry, found that they protected mice from otherwise fatal hemolytic streptococcic infections. Both these preparations were called prontosil.

Such was the beginning of what has proved to be the greatest contribution to chemotherapy. Later in 1935 Levaditi and his co-workers at the Pasteur Institute, using similar compounds synthetized by Girard, were able to confirm Domagk's work. But, also they were the first to suggest that the active chemical substance of the dye was really sulfanilamide, the same preparation which had been prepared by Gelmo twenty-seven years previously. The favorable clinical and bacteriologic report of Colebrook and Kenny in England early in 1936 on the use of the prontosils in puerperal fever really awakened the wide interest in these new chemotherapeutic preparations. In this country the report in 1937 of Long and Bliss of their work with the prontosil dyes and sulfanilamide added much to our experimental and clinical knowledge as to dosage and types of infection for which they were effective. Since then, the number of both clinical and experimental investigations that have been reported are too numerous to mention. This literature includes theories of modes of activity of these drugs, dosage and methods of administration, toxicity and complications, and their therapeutic properties for most types of organisms and infections. Several scores of sulfanilamide derivatives and related compounds have been prepared, but most of them have had to be discarded for the present at least because of their toxicity. To date only sulfanilamide, neoprontosil, sulfapyridine, and sulfathiazole can be recommended for general use.

As yet we do not know the mechanism of action of these chemotherapeutic agents. When that is solved, there undoubtedly will be a further great development in chemotherapy.

The Mechanism of Chemotherapy*

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The mechanism of action of chemotherapeutic agents is not yet definitely known, although many theories have been proposed and many important observations have been made. Long and Bliss[1] list 151 references at the end of their chapter on "The

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Mode of Action of Sulfanilamide and Its Derivatives," and many important articles have appeared since their monograph was published. It is obvious, therefore, that a complete review of the subject is not possible within the time limits of a round table discussion. Only a few of the important references can be cited, but references to other work will be found in these and in the review by Long and Bliss.[1] Since most of the investigators, including myself, who have studied these agents over a period of time have revised their theories from time to time as more data have been accumulated, even the most recently published theory of an investigator may not represent his present view.

Since observations are much less likely to be in error than conclusions derived from these observations, I will first summarize certain observations on which there is reasonably good agreement. Most of the illustrative examples were chosen from my own studies, although, as a rule, similar observations have been made by many others.

Any theory which is to explain the action of these chemotherapeutic agents must also explain these observations. The number of organisms present has a great influence on the effectiveness of the drugs. Small inoculations may be sterilized by a concentration of the drug which has little effect on the growth of a larger inoculation under otherwise identical conditions.[2] Slight differences in environment or medium may lead to great differences in the effectiveness.[2] A drug which is effective against a particular organism in the blood of one species may be relatively ineffective in the blood of another species. An inoculation of beta hemolytic streptococci in Hartley broth was not sterilized by ten times the concentration of sulfanilamide which sterilized four hundred times as large an inoculation of the same organism in marrow culture. There is an initial lag period of two to six hours after addition of the drug before any evidence of its effect on the rate of growth of the organism is detected.[2] When the concentration of the drug and other conditions are such that sterility occurs, a considerable period of time, often several days, may elapse after the effect of the drug has become evident before sterility is complete, and under some conditions, either in cultures or in animals, small numbers of organisms may be present for long periods of time in the presence of the drug without becoming numerous or being completely killed.[3] Widely different organisms may respond to the same drug, but organisms thought to be closely related may show wide differences in response. Sulfanilamide is of definite value against such widely different organisms as the beta hemolytic streptococcus and *Clostridium welchii*;[4] yet one strain of pneumococcus of the same type may be resistant to a concentration of sulfapyridine which is effective against most strains of the same type of pneumococcus.[5] An organism at first highly susceptible to the drug may become resistant after repeated passage through cultures containing the drug,[6] although as a rule susceptible organisms, if inoculated into cultures containing the drug in large enough numbers to survive, are still susceptible to the action of the drug on small inoculations.[2] Changes in the para-amino group tend to alter the activity of the compounds without changing strain specificity; thus, the acetyl derivatives[3a] or the corresponding ortho- and meta-amino compounds are inactive.[7] Changes in the sulfonamide group tend to alter the strain specificity of the compounds; thus, sulfanilamide is only slightly effective against the pneumococcus, while sulfathiazole and sulfapyridine are very effective.[8] Sulfathiazole is far more effective than sulfapyridine against the *Staphylococcus aureus*. Neoarsphenamine, which is widely different in composition, is highly effective against the *Staph. aureus*.[9] Variations in temperature have a tremendous effect on the action of these drugs.[10] At icebox temperature the organisms fail to grow and there is no effect of either neoarsphenamine or sulfathiazole on staphylococci; at room temperature, at body temperature, and at 41° C. these drugs are effective. Woods[11] has shown that p-nitro-benzoic acid inhibits the action of sulfanilamide. Under

certain conditions peptone interferes with the action of these drugs,[12] and under other conditions this is not the case.[13] Toxin accumulation may be less in the presence of the drug than without it.[2] The combined effects of the drug and specific antibodies may be much greater than either alone, but complete sterilization may occur in the absence of antibodies.[8] The presence of leucocytes is not essential for the action of the drug, but they may have a decisive effect on the outcome of a particular infection. Susceptible organisms in the presence of these drugs may develop definite changes in morphology[4] which do not occur in control cultures. These changes include a tendency to chain formation, swelling of the organisms, and alterations in staining properties, but not loss of capsules.

Many theories have been proposed to explain the mechanism of the action of chemotherapeutic agents. The view that the drugs in some way act on the organisms or cells to promote phagocytosis and that the killing of the organisms is due solely to phagocytosis is disproved by the fact that sterility may occur in the absence of leucocytes and that exposure of organisms or cells to the drugs has little effect on phagocytic activity.

The theory that the action of the drug is simply bacteriostatic or that it decreases the rate of cell division seems untenable in view of the actual sterilization of considerable inoculations in the absence of leucocytes and antibodies and the fact that definite changes in morphology of the organism occur. The view that the effect is on the capsules of the organisms, rendering them relatively avirulent, is disproved by the observation that capsules are still intact in organisms that have been exposed to these drugs and that the organisms retain their virulence after exposure to the drugs.

The opinion which I first held, that the organism was merely rendered more susceptible to the action of antibodies and that antibodies were essential for sterilization,[2b] has been disproved by the fact that sterilization may occur in the absence of both leucocytes and antibodies, although there is abundant evidence that sterility is more likely to occur if antibodies are also present. While less toxin accumulates in the presence of the drug, preformed toxin is not significantly inactivated by these drugs,[15] and the morphologic changes in the organism and sterilization in the absence of leucocytes or antibodies indicate that this is not the major action of the drug.

The presence of the lag period before the action of the drug becomes evident has suggested to many investigators the possibility that before action takes place, the drugs must first be changed to some other compound. There seems to be little conclusive proof either for or against this theory at the present time, although if such a change occurs it must involve a relatively small percentage of the drug present and be a reversible reaction, because most of the drug present can be recovered after the effect has occurred either in unaltered form or in the form of the acetyl derivative which has been shown to be ineffective. The lag period could be explained equally well as representing the time necessary for a chemical reaction between the drug and the organism to occur, for even the effects of many mammalian poisons do not become manifest for long periods of time.

The theory that the killing of the organisms is due to accumulation of hydrogen peroxide produced by the organisms and made possible by the inactivation of catalase by the chemotherapeutic agents has some support in that it has been shown that catalase may be partially inactivated by these drugs and some of their derivatives.[16] It is hard for me to see, however, why, if the organisms are killed by anything which they themselves produce, there would not be a more rapid death of organisms the larger the inoculation; whereas, the exact opposite is true. It is also hard to understand why the organisms would not produce enough hydrogen peroxide to kill themselves in a medium devoid of catalase and how enough hydrogen peroxide could accumulate in our marrow cultures to kill the organisms in the pres-

ence of red cells and leucocytes, both of which tend to decompose hydrogen peroxide very rapidly. Furthermore, if the action is on catalase and not on the organisms, it is hard to explain the differences in effectiveness of the different derivatives against the different organisms.

The theory that the action of the drug is to inactivate a proteolytic enzyme present in virulent organisms which is responsible for their ability to grow on medium devoid of protein-split products and in the human body has been advanced by Lockwood,[12] because he observed that under certain conditions the presence of peptone interfered with the action of the drugs. However, we have been able to obtain complete sterility in marrow cultures containing 25 mg. per 100 c.c. of neopeptone. Others also have demonstrated that sterilization may occur in the presence of peptone.[13]

Shaffer[17] has recently suggested that the production of peroxide by the organisms oxidizes the drugs to the hydroxylamine or nitroso derivatives, which are themselves highly unstable and powerful oxidizing agents, and that these raise the oxidation-reduction potential of the medium above a critical level which is necessary for the life of the organism. This is difficult to correlate, however, with our observations,[18] that the presence of a powerful reducing agent, such as sodium formaldehyde sulfoxalate which in itself has no sterilizing action, does not interfere with and possibly enhances the effects of sulfathiazole, while the addition of hydrogen peroxide does not increase the effectiveness of these drugs in marrow cultures. Much further work is obviously desirable on the effects of oxidizing and reducing agents on the effectiveness of these compounds.

At present it seems to me probable that these drugs act directly on the organisms, producing definite changes in morphology and ultimate death; that this process requires considerable time; and that the most probable explanation for the ineffectiveness against large numbers of organisms is that the organisms tend to produce something, possibly para-nitro-benzoic acid, as suggested by Woods,[11] which inactivates the drug. The structure and function which are poisoned in the organisms are still undetermined, as is the reason for the lag period.

The facts that are known about the action of these drugs indicate the importance of starting therapy early while the numbers of organisms are still small, of choosing the drug which is most effective against the particular organism, of giving the drugs frequently enough to maintain the desired concentration without interruption, of giving therapy designed to introduce or to stimulate the production of antibodies if the drugs alone do not prove effective, of continuing therapy for several days after the infection is apparently cured, and of draining local collections of pus and introducing the drugs locally where the organisms are likely to be numerous. They suggest the possibility that associated fever therapy will sometimes prove effective when the drugs alone are ineffective and offer hope that many other compounds of chemotherapeutic value may be discovered.

Summary

The mechanism of the action of chemotherapeutic compounds on bacterial infection is not yet known. There are serious objections to most theories of the action so far proposed. Some of the observations which must be explained by any theory of the action of these drugs are reviewed, and some general principles based on these observations which should govern the clinical use of these drugs are given.

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Chemotherapy of Acute Infections

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The discussion of the problems of chemotherapy of acute infections was introduced according to the following scheme:

I. Selection of Drug, Bringing Up the Question of

(1) The empirical use of drugs with broad coverage in:

a. Early acute severe infections, the bacterial etiology of which may not be established for from twelve to thirty-six hours, or longer.

b. "Mixed" infections.

(2) Substitution of one drug for another on clinical grounds.

(3) Combination of two or more drugs with or without antisera.

(4) Scientific selection of drugs. Methods.

a. Effectiveness

b. Toxicity

II. Methods of Drug Administration Other Than by the Oral Route.
III. Optimum Drug Concentrations.
IV. Discontinuation of Chemotherapy.

1. As well as could be ascertained, a majority believed that, except in the cases of known sensitivity to the particular drug or drugs later mentioned, it seems best to treat all acute infections by chemotherapy as early as possible, since there is ample evidence to indicate that the effectiveness of chemotherapy varies not only directly with the concentration of the drug, but inversely with the number of organisms which have to be destroyed (which often is proportional to the duration of the infection, number and severity of complications, amount of inflammatory exudate, etc.).

2 In those infections in which the bacterial etiology has not yet been established, therefore at the beginning of most acute infections and even in most complications where it is possible that an organism other than the original one may be the cause of the complication (as, for instance, pneumonia complicating scarlet fever or hemolytic streptococcic otitis media, which often is due to the pneumococcus), it seems best to begin therapy with a drug of "broad coverage," which at present means either sulfapyridine or sulfathiazole. Exception may be made and sulfanilamide may be selected as the first drug for infections whose etiology is apparent, such as typical scarlet fever and typical erysipelas (but not the "erysipeloid" of nephrosis, where the infecting organism is not always the hemolytic streptococcus, but may be a pneumococcus or a colon bacillus). A similar exception may also be made when infection complicates nephritis or renal insufficiency, if one considers sulfanilamide a safer drug from the standpoint of possible further renal injury.

3. Comparing sulfapyridine with sulfathiazole, the following seems to be true: (a) In pneumococcic pneumonia sulfapyridine seems a little more effectual (the temperature falls a little sooner and perhaps there are fewer complications such as empyema and otitis media); (b) in meningitis, sulfapyridine should also be preferred because it diffuses more readily into the spinal fluid than does sulfathiazole; (c) the greater tendency of sulfapyridine to promote vomiting should not of itself favor the selection of sulfathiazole since adequate sulfapyridine therapy may be effected by intravenous administration (0.5 to 2.0 c.c. per kilogram of a 5 per cent solution of sodium sulfapyridine given every 8 to 12 hours) or by rectal administration every 6 hours of a 2 per cent solution of sodium sulfapyridine in doses comparable to those administered orally as sulfapyridine, and (d) clinical results in staphylococcic infections seem not to favor sulfathiazole as much as do test tube and animal experiments.

4. The best chance of eradicating infection quickly, preventing troublesome complications and "acquired fastness" to the drug by the organism, seems to lie in early intensive treatment (heavy dosage, parenterally administered if necessary and locally on occasions) with diminution of dosage as soon as clinical and laboratory findings seem to justify such a step. In meningitis daily dosage of 0.4 to 0.6 Gm. per kilogram is often indicated.

5. Use of more than one drug at a time may sometimes be advantageous, especially if one is used chiefly because of ease of parenteral administration or to achieve high concentration by local injection (as, for instance, by injecting sulfanilamide intrathecally or into joint cavities).

6. There is need of a good method for scientific selection of drug and optimum concentration for each severe infection if it seems refractory to treatment. At present one certainly is justified in alternating drugs and being guided by clinical response.

7. The optimum time of discontinuation of chemotherapy is also still arrived at largely empirically.

Chemotherapy of Urinary Infections

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The chemotherapy of the infections of the urinary passages has made great progress in the last decade. From 1895, when Nicolaier first introduced methenamine as a urinary antiseptic, up until 1931 when Clark and I introduced the ketogenic diet for the treatment of urinary infection, no drugs were introduced that have proved superior to methenamine. Hexylresorcinol, serenium (2, 4-diamino-4'-ethoxy-azobenzene hydrochloride), and pyridium (phenylazo-*aa*-diaminopyridine monohydrochloride), to mention only a few of this series of drugs, have fallen largely into disuse as urinary antiseptics. The same can now also be said of the ketogenic diet, because the active drug, beta-oxybutyric acid, has been replaced by another organic acid that can be administered much more easily. This organic acid, mandelic acid, was introduced by Rosenheim in 1935 and has taken the major place of those urinary antiseptics that require a definite urinary acidity to develop their bactericidal power.

As Rosenheim has shown for both beta-oxybutyric acid and mandelic acid, the bactericidal power of the urine varies with the concentration of free undissociated acid. The free undissociated acid varies directly with the concentration of the acid in the urine, and inversely with the pH. Only 0.25 per cent of the acid is necessary for bactericidal action at pH 5.0, 0.5 per cent is necessary at pH 5.5, 2.4 per cent is necessary at pH 6.0, and 24 per cent at pH 7.0. It is thus immediately evident that with a daily maximal adult dose of 12 Gm. and a urinary output of about 1,000 c.c., the maximal concentration could be only 1.2 per cent even if all of it were excreted in the urine. This would require a pH considerably less than 6.0 for bactericidal action. Practically, it is necessary to have a urine of pH 5.5 in order to get a bactericidal urine with the usual dose. I like to indicate the dose for children as 1 Gm. of calcium mandelate for each 100 c.c. of urinary output in twenty-four hours. This usually is sufficient to give the urine the necessary concentration of acid and a pH less than 5.5.

It will be noted that methenamine, the ketogenic diet, and mandelic acid all require a definite acidity for the development of their actions. The necessary level seems to be at or about pH 5.5. The attainment of this level is the stumbling block in the treatment of many urinary infections. Two distinct groups are here to be recognized: The group in which the kidney, because of reduced function, cannot excrete the drug in sufficiently high concentration or cannot excrete a urine of low pH, or both; and the group in which the infecting organism produces an alkalinity of the urine which persists in spite of the administration of acid and acid-forming salts. This deficiency is of particular significance when we realize the frequency with which unilateral involvement occurs in kidneys damaged by obstruction or infection, or both. Even when the combined bladder urine reaches the proper degree of acidity and concentration of the drug, the affected kidney may be excreting a urine of high pH and low concentration of the drug. An organic acid which in the same concentrations would give a bactericidal urine at a higher pH would be very desirable.

In 1936 prontosil was first used as a urinary antiseptic and the following year it was shown that sulfanilamide, split off in the body, was excreted by the kidney to produce a bactericidal urine. Even in very low concentrations this drug was very effective in the treatment of infection with the gram-negative bacilli. The large doses given at first have gradually been replaced by smaller doses that are unlikely to give toxic effects. With doses as low as 30 gr. (2 Gm.) for the adult, numerous observers have been successful in getting rid of an infection in a few days. Our regular dose has been ½ gr. (0.032 Gm.) to the pound for infants and smaller children, and a maximum of from 30 to 40 gr. (2 to 2.6 Gm.) for older children.

Sulfanilamide is excreted in the free and the conjugated form, but only the drug in the free state is bactericidal. The two forms are usually excreted in about equal amounts. Even the damaged kidney can excrete sulfanilamide in bactericidal concentrations, so that it is a drug that can be used successfully in infections of patients with a blood urea greater than 50 mg. in 100 c.c. The phenolsulfonephthalein output and the sulfanilamide output parallel each other. The one great handicap of sulfanilamide is its total failure to act on *Streptococcus fecalis*. Sulfapyridine has this same handicap. Before the use of sulfanilamide, *Str. fecalis* seemed to play a very minor role in the causation of pyuria, but since the introduction of sulfanilamide it has been found that with the disappearance of the gram-negative bacilli from a grossly contaminated urine, *Str. fecalis* is not infrequently found as a solitary survivor. Two patients recently admitted with posterior urethral obstruction had pure *Str. fecalis* infection. The one had been treated previously with sulfanilamide and the other with sulfapyridine. Reaction of the urine does not seem to play an important role in the action of sulfanilamide, as there are experiments that seem to show an advantage for its action in acid urine and others for its action in alkaline urine. It is to be emphasized that there is as great variation in the susceptibility of various strains of the same bacterium to the drug as there is variation in the susceptibility of the different bacteria.

The most recent sulfone compound that has been used as a urinary antiseptic is sulfathiazole. In testing out this substance for its antiseptic properties, I was able to show that its action on the usual gram-negative bacilli found in urinary infections was equal to that of sulfanilamide and that in addition it did act on *Str. fecalis*. Some observers have classed sulfathiazole with sulfanilamide, but a number of observers have shown it to be of definite value in *Str. fecalis* infection. Just recently I have completed a large series of determinations on the bactericidal power of sulfathiazole. In brief my results are as follows:

Staph. aureus is killed off in the lowest concentrations. A concentration of 25 mg. in 100 c.c. of urine kills off practically all strains; 6.25 mg. in 100 c.c. is bactericidal for some strains. *Proteus ammoniae* is next in order the most easily affected bacterium. Fifty milligrams in 100 c.c. is bactericidal in most determinations. *Aerobacter aerogenes* and *Escherichia coli* are both affected in low concentrations of sulfathiazole but many strains are not killed off until concentrations of 150 mg. in 100 c.c. are reached. *Str. fecalis* is definitely more resistant. It is killed in much lower concentrations in urine at pH 5.5 and 6.5 than at pH 7.5. *Pseudomonas aeruginosa* is the most resistant bacterium, requiring up to 300 mg. in 100 c.c. for a bactericidal effect.

Summary.—We have at present three good urinary antiseptics, mandelic acid, sulfanilamide, and sulfathiazole, any one of which should clear up the average urinary infection in the course of a week. Even with urinary obstruction, many infections can be cleared up unless there is lowered function in one or both kidneys. With damaged kidneys, sulfanilamide and sulfathiazole are the drugs of choice. In *Str. fecalis* infection sulfanilamide is of no value.

The subject under discussion is so distinctly one of the effect of chemotherapeutic drugs on bacteria that I have limited myself in the discussion to diseases of the gastrointestinal tract caused by bacteria.

Neoprontosil has proved of definite value in the treatment of chronic ulcerative colitis, particularly of type I, in which the Bargen streptococcus seems to play a role. Adults and older children received from 3 to 4 Gm. (45 to 60 gr.) a day for two weeks; children from 5 to 10 years of age, 1.5 to 2.5 Gm. (22 to 37 gr.) in twenty-four hours for two weeks.

Marshall has recently published experimental studies on the use of sulfanilylguanidine on typhoid and dysentery bacillus. At present no published clinical work is available to show its possible therapeutic use in man.

Dangers and Disadvantages of the Sulfonamide Drugs

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The introduction of the sulfonamide drugs into the chemotherapy of acute infections naturally found the medical profession expectant of undesirable reactions. It seems perfectly reasonable to fear that a drug which aids the destruction of dangerous bacteria should have serious effects upon the human body. The use of these drugs in childhood was attempted with especial timidity lest children be found to be even more susceptible than adults to dangerous toxic effects. Accumulated experience with these drugs has demonstrated, however, that few serious side effects are to be expected, that these deleterious effects are even less common in children than in adults, and that, almost without exception, serious reactions can be anticipated and prevented by intelligent supervision and a properly planned scheme of therapy. Perrin Long, in a recent summary of the reactions to these drugs, is responsible for the statement that "physicians have been oversold on the dangers connected with the use of sulfanilamide and its derivatives and . . . these drugs can be used with greater impunity than has hitherto been considered possible."

Some of the dangers, the seriousness of which has been overemphasized, are cyanosis, the combined use of other drugs including the sulfate, the possibility of inducing hypersensitivity, gastric intolerance, and central nervous system involvement; they are more common in adults than in children.

Apart from the dangers which have been overrated there are a few effects which do deserve consideration. Almost without exception serious difficulties can be obviated by intelligent supervision designed to detect reactions before they can progress.

The blood needs careful watching. Almost invariably a careful blood examination should be done before treatment is started; this will guard against the use of the drugs in the acute blood dyscrasias, leucemia, agranulocytosis, infectious mononucleosis, etc., in which it is not uncommon to see chemotherapy administered on purely empirical grounds because of the appearance of the throat. After treatment is started, examination of the patient will usually give warning of dangerous effects upon the blood, but the routine of a blood count twenty-four hours after treatment is begun and at suitably frequent intervals thereafter is a desirable precaution. A rapid reduction in red cells or in granular white cells may occur during the first few days and merit prompt recognition with, usually, a discontinuation of therapy. As therapy continues there is usually a gradually progressive hemolytic anemia, but at any stage a sudden severe granulocytopenia or hemolytic anemia may supervene. More rarely, especially in association with acute hemolytic anemia, an extreme leucocytosis may occur which Long explains as being due to extreme demands upon the bone marrow. Not only may either red or white cells be affected, but the blood platelets may be reduced with the production of purpura hemorrhagica. That adverse effects have been reported more with sulfanilamide and sulfapyridine than with sulfathiazole possibly indicated only a lesser experience with the latter drug.

A variety of rashes have been reported from these drugs. It has not always been easy to differentiate rashes which are a part of the disease from those which are due to therapy, but there is no doubt that rashes have occurred with the use of all these drugs and usually indicate that one should proceed with caution or terminate the therapy.

These agents occasionally themselves cause fever and almost invariably it has been difficult to determine whether fever has been due to the drug or to the disease. It may not be possible, except by a method of trial and error, to determine the cause of fever, but usually drug fever appears toward the end of the first week of treatment after the full height of therapeutic effect is reached and

when symptoms otherwise tend to abate. At this stage, in the majority of instances, the drug can be withheld and subsequent treatment based on the response of the patient.

A number of different factors should be comprehended in this plan. An initial consideration is that diagnostic study should be adequate. It is usually possible to determine the need for these drugs from history and physical examination, and it is often desirable to initiate treatment on the basis solely of clinical considerations. Before therapy is actually started, however, specimens should be collected for throat culture, blood culture, pneumococcus typing, etc., for often the progress of the patient makes it extremely essential to have such information which it may be difficult later to secure. It is rarely necessary to begin treatment without a preliminary blood count. This initial count also serves as a base line for comparison with subsequent counts; this may help to clarify the question, as therapy proceeds, whether changes in the blood are the results of disease or of treatment.

After the diagnosis is satisfactorily established, the clinician must decide upon the advisability of chemotherapy and the particular drug which should be applied. This is not purely a question of etiology, for many bacterial infections which are susceptible to chemotherapy are sufficiently mild as not to justify the risk and discomfort of this treatment and may best be served by only symptomatic care. I find sulfanilamide sufficiently unpleasant in its effects that I should not have cared to take it for the majority of my own past streptococcus throat infections.

The use of chemotherapy should be determined with respect to the pathology as well as the etiology. There is no doubt that sulfanilamide is active against the scarlet fever streptococcus but its bacteriostatic powers are most useful at the very onset and at the later stage of bacterial invasion. The drug has no antitoxic activity, however, and at the height of the toxemia, and rash, it is better to use a potent antitoxin in preference to a more slowly acting bacteriostatic agent.

The situation is almost identical with respect to meningococcus disease. The situation with regard to pneumococcus, staphylococcus, and other bacterial infections is somewhat less clear cut, although study of the patient will often determine conditions which indicate use of immune serum instead of, or in combination with, the chemical agent.

Having decided upon the use of one of these drugs, it should be given in adequate dosage and at regular intervals. With optimum dosage it is usually possible to determine quickly the therapeutic effect and many infections may be almost entirely controlled during an interval when there is little likelihood of serious toxic effects from the drug. Heroic dosage is usually unnecessary, but these drugs should invariably be given so as to secure quickly full therapeutic effects. The determination of blood levels is a helpful, although somewhat variable, guide; careful observation of the patient is more essential. Having determined that improvement is brought about by the drug, its administration may then be continued as needed and as tolerated.

In conclusion it may be said that the dangers incident to therapy with the sulfonamide drugs are not sufficient to dissuade one from their use in any condition in which they are indicated. Many of the dangers are fancied rather than actual, and the bona fide dangers can mostly be obviated by adequate and intelligent supervision. As a preliminary to treatment there should be an exact diagnosis and a clear-cut concept of the disease mechanism. The danger of treatment should be weighed against the potential seriousness of the disease. The drugs should be administered in effective dosage; one should not mistake timidity or uncertainty for conservatism. During the period of treatment the patient should have watchful care supplemented by judicious laboratory procedures.

DISCUSSION

DR. J. K. EVERHART, PITTSBURGH.—Which is more effective in type III pneumonia, sulfapyridine or sulfathiazole?

DR. HARTMANN.—Our results were poor in type III pneumonia.

CHAIRMAN TOOMEY.—I advise large doses of serum and sulfapyridine.

DR. N. T. WELFORD, LA GRANGE, ILL.—Has stovarsol or other arsenicals given by mouth been tried in staphylococcic infections?

DR. OSGOOD.—While stovarsol had not been tried, other arsenicals tried had not been as effective as neoarsphenamine.

DR. HUGHES KENNEDY, JR., BIRMINGHAM.—Can the sudden drop in temperature which occurs in the use of sulfapyridine be due to purely antipyretic effect?

DR. HARTMANN.—I doubt it because of the failure to demonstrate antipyretic effect in such diseases as typhoid and influenza where the drug has no therapeutic effect.

DR. G. L. DRENNAN, JACKSONVILLE, ILL.—Should sulfanilamide be used in scarlet fever?

CHAIRMAN TOOMEY.—It is effective especially in the complications, even in the presence of nephritis. The toxemia does not respond to sulfanilamide. Serum with its antitoxic effect is more effective in the early stage. If sulfanilamide is given for mastoiditis, roentgenograms should be taken to follow its course.

DR. HARTMANN.—I favor the use of sulfanilamide early in scarlet fever. The early toxic phase does not kill. It is more like a sensitive phenomenon. It is the infectious phase that kills. In 300 cases of scarlet fever in which 0.2 Gm. per kilogram of sulfanilamide was given until temperature was normal for two days, there were no deaths and fewer complications except for nephritis. Probably a combination of serum and sulfanilamide would be best.

DR. W. A. McGEE, RICHMOND, VA.—What is the percentage of probable error in pneumonia statistics since most children get well without chemotherapy?

DR. K. D. BLACKFAN, BOSTON.—The economic factor is also important. A shorter hospital stay and fewer complications as well as relief from anxiety of both parents and doctors make chemotherapy worth while.

DR. R. W. HOLT, NIAGARA FALLS, N. Y.—Is chemotherapy effective in measles and pneumonia?

CHAIRMAN TOOMEY.—Sulfapyridine is effective in pneumonia complicating measles and also in that complicating whooping cough.

CHAIRMAN TOOMEY.—Dr. Helmholz, will you comment on the value of potassium citrate in urinary infections?

DR. HELMHOLZ.—I do not believe alkalies are of any value in treating urinary infections. Furthermore, acid urine is definitely less irritating to the bladder than alkaline urine.

DR. BIGLER.—Are alkalies of value in acute pyelitis?

DR. HELMHOLZ.—The majority of acute pyelitis cases in children get well with no therapy. The normal washing of the urine is effective.

CHAIRMAN TOOMEY.—What is the drug of choice?

DR. HELMHOLZ.—Sulfathiazole, ½ gr. to the pound in twenty-four hours. You can expect results in from twenty-four to forty-eight hours. If there is no response in this time, the urine should be cultured and mandelic acid tried, preferably as calcium mandelate.

CHAIRMAN TOOMEY.—What drug would you use in acute hemorrhagic nephritis?

DR. HELMHOLZ.—Sulfanilamide. Thirty grains a day is enough for an adult. High blood concentrations are not needed.

DR. W. L. CRAWFORD, ROCKFORD, ILL.—How can one distinguish between drug fever and fever due to infection?

DR. HARTMANN.—In meningitis the spinal fluid examinations reveal the cause of the fever. In other conditions the differential blood count is of help.

DR. S. H. ASHMUN, DAYTON, OHIO.—What use has neoprontosil in chemotherapy?

DR. HELMHOLZ.—It is of definite value in chronic ulcerative colitis. Only that portion of the drug convertible into sulfanilamide is useful. That would be about 11 gr. in 100 c.c. of 2½ per cent solution.

DR. J. K. MACK, LOUISVILLE.—How effective is sulfathiazole in treating dysentery?

DR. HARTMANN.—I have been disappointed in our cases of the Hiss, Russel, and Flexner types.

DR. W. E. KEITER, KINSTON, N. C.—I see approximately 100 cases of dysentery a year. Before I used sulfanilamide, I had a mortality of 6 to 8 per cent. With the aid of sulfanilamide and starvation, I have had one death in three years. My cases were not cultured.

Proceedings

ELEVENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

BOSTON, MASS.—OCT. 9-11, 1941

Minutes of the Meeting of the Executive Board (Oct. 8, 1941)

The following were elected to Fellowship:

Region I

Mary Adams, Riverside, Conn.
Louis Appel, Flushing, N. Y.
Robert H. Detwiler, Washington, D. C.
Richard A. Downey, Buffalo, N. Y.
J. Harry Ebbs, Toronto, Ont., Canada
A. P. Hart, Toronto, Ont., Canada
Thomas M. Lamb, Brooklyn, N. Y.
Harold Levy, Brooklyn, N. Y.
John H. McLeod, Washington, D. C.
Robert Taylor Moulton, Salem, Mass.
David Stewart Polk, Rosemont, Pa.
Laurence G. Pray, Washington, D. C.
Howard G. Rapaport, New York, N. Y.
Thomas Eugene Shaffer, New Haven, Conn.
John A. Washington, Washington, D. C.
Sidney H. Weiner, Boston, Mass.
Alfred Weller, Arlington, Mass.
L. Holland Whitney, Brooklyn, N. Y.

Region II

Merrill W. Everhart, New Orleans, La.
Albert Mitchell Jones, Memphis, Tenn.
Thomas Stanley Meade, Richmond, Va.
Halcuit Moore, Dallas, Texas
Owen S. Ogden, Louisville, Ky.
Thomas S. Weaver, Nashville, Tenn.

Region III

Marion L. Ainsworth, Columbus, Ohio
Arild Edsten Hansen, Minneapolis, Minn.
Theodore P. Herrick, Cleveland, Ohio
E. O. Jodar, Detroit, Mich.
Howard T. Knobloch, Bay City, Mich.
Kenneth W. A. McLeod, Lapeer, Mich.
Tracy D. Peppers, Greeley, Colo.

Region IV

Edwin R. Cole, Sacramento, Calif.
Helen Hopkins, Los Angeles, Calif.
Willard B. Rew, Yakima, Wash.

Alfred C. Henderson, Stamford, Conn., elected to Emeritus Fellowship.

The following were elected to Associate Fellowship:

Thomas H. Lanman, Boston, Mass.
James S. Plant, Newark, N. J.
Harvey Spencer, Boston, Mass.

It was voted that the Publicity Service be continued for another year at the same cost.

The following were elected Associate Chairmen:

Region I, Dr. Lewis Webb Hill
Region III, Dr. George F. Munns

Dr. Hugh McCulloch was named to succeed Dr. Borden S. Veeder on the American Board of Pediatrics.

At the request of the Chairman of the Committee on Postgraduate Education, it was voted that $50.00 be paid to the Associated States Postgraduate Committee for the continuation of our cooperative relationship.

It was voted that a book on the policies of the Academy be prepared by Dr. Ernest Caulfield for the use of future presidents and that a book on policies for annual meetings be prepared by the Secretary and Assistant Secretary for local committees on arrangements.

The following resolution was passed by the American Legion at its recent meeting in Milwaukee:

> THEREFORE BE IT RESOLVED, that the American Legion approves such co-operative relationship of the American Legion National Child Welfare Division with the American Academy of Pediatrics as may be developed after complete study by the National Child Welfare Division

of all of the conditions involved and instructs the National Child Welfare Commission, the National Child Welfare Division and the Departments to make full use of the services offered by the American Academy, for which services there will be no financial or other obligation on the part of the American Legion, its National, Department, or Post organizations, and in so far as possible the Pediatrician be a member of the American Legion.

All the Committee reports were accepted and approved.

It was the consensus of the Executive Board that the expenses of both the Regional and Associate Chairmen to regional meetings should be met; the national association to meet half of this expense, provided the regions met a proportionate share.

Chicago was recommended for the next place of meeting.

Report of the Secretary

The past year in the Academy has been represented by several different tendencies and activities which are noteworthy.

In the first place, there has been a very definite tendency for the regional meetings to be put on a business basis and to develop independently. In the second place, there has been more activity in the states and the State Chairmen have become more and more interested in their work.

We have lost seventeen men in Service. These are all that have come to the attention of the Secretary. There may be more. The Committee on National Defense has been very active and has done some notable things. The children from foreign countries who were to be placed in this country have been examined at ports of entry and all this work has been under the supervision and active participation of members of the Academy, and directed by this Committee. At the request of Dr. Joseph Stokes and Dr. Martha Eliot, there has been prepared a list of those men who had one or two years' training in pediatrics during the last five years. This list, of course, is not absolutely complete, but so far as we can determine it must be close to 95 per cent. In addition to this, the Committee on National Defense is considering the evacuation of cities on the east coast and the placing of children from these cities in case such evacuation is necessary.

Of the work of the special committees, the work of one, the results of which are not so evident to members of the Academy, is that of the Committee on School Health. In its quiet way it is slowly, but surely, having a very decided influence on the school health situation in this country. Slowly, but surely, the authorities who have this in hand are coming to the views expressed in the report of this Committee, and the Secretary's office is receiving more and more requests for copies of this report.

The Committee on Cooperation with Nonmedical Groups has arranged to have printed two pamphlets; one for physicians, and one for laymen, to be distributed at the showing of the film, "When Bobby Goes to School."

The cooperation with the American Legion is becoming closer and will probably blossom forth with the appointment of state liaison officers for this group.

The Committee on Mental Health is preparing a film, the scenario of which will be submitted to the Academy members. This film is to be financed by the Pet Milk Company.

The Committee on Central and South American Scholarships has gotten well under way and after some difficulties which were in no way due to either collection of funds or the activities of the Committee, it has finally placed several South American physicians in this country and has prospects for several more.

The Council for Pediatric Research has been reorganized on a different basis and in the future will act largely in an advisory capacity.

Dr. Edgar E. Martmer, Assistant Secretary, has prepared a manual for State Chairmen which we hope will be of value.

The Academy now has 1396 active members, of which 72 were elected this year. During the past year, the Academy has lost through death and other causes fifteen members. It is the sad duty of the Secretary to report the deaths of the following:

Dr. Paul B. Bender, Philadelphia, Pa.
Dr. Paul H. Herron, Oak Ridge, La.
Dr. E. A. Hines, Seneca, S. C.
Dr. Thomas D. Jones, Richmond, Va.
Dr. G. W. Kutscher, Jr., Asheville, N. C.
Dr. A. Graeme Mitchell, Cincinnati, Ohio
Dr. Fred Moore, Des Moines, Iowa
Dr. Robert G. Sharp, San Diego, Calif.
Dr. Henry L. K. Shaw, Albany, N. Y.
Dr. Charles A. Wilson, Detroit, Mich.

Respectfully submitted,
CLIFFORD G. GRULEE
Secretary

Treasurer's Report

STATEMENT OF RECEIPTS AND DISBURSEMENTS
July 1 to September 15, 1941

Balance, July 1, 1941			$ 7,282.15
Receipts:			
Dues		$13,069.13	
Annual meeting:			
Exhibits	$1,167.50		
Clinics	434.00	1,601.50	
Interest on Bonds		190.83	
Pamphlets		53.40	14,914.86
			$22,197.01
Disbursements:			
Salaries:			
Secretary	$1,800.00		
Assistant Secretary	300.00		
Stenographer	480.00		
Office	147.35	$ 2,727.35	
Subscriptions		6,745.00	
Publicity		750.00	
Annual Meeting		167.50	
Executive Board		10.00	
Rent		300.00	
Postage		248.14	
Telephone and Telegrams		102.17	
Exchange and Charge on checks		66.74	
Treasurer's Bond		62.50	
Travelling Expense (Secretary)		41.82	
Office Supplies		41.23	
Certificates		29.20	
Stationery and Printing		21.00	
Miscellaneous		13.06	
Refund for Clinics		2.00	
Expense:			
State	$ 26.33		
Committee	15.40	41.73	11,369.44
Balance, September 15, 1941			$10,827.57

Fellows	1396
Dues paid	1088
Dues unpaid—1941-1942	308
Dues unpaid—1940-1941	28

Report of Region I

For several years past, complete annual reports have been rendered in considerable detail as to the general progress of Academy activities in Region I, together with highlights of special activities being carried on in our states and provinces.

Because of the large amount of mimeographing in connection with the preparation of outlines of duties of National and State committees, Regional and State Chairmen, etc., request has been made for as much condensation of all reports as is possible this year. Therefore, this report will be so condensed. Fellows interested in more detail of our Regional or State activities are therefore referred to previous reports and to the State and Province Chairmen's 1941 reports which will be available at our Boston meeting.

Region I, with the aid of its officers, State Chairmen, Committees, and Fellows, has continued to make steady progress this year toward the objectives of the Academy.

At National and Regional levels, the Academy is making commendable progress. What is now most needed is the further improvement of Academy activities within each of our states and provinces and increased opportunity for each Fellow to participate in some worthwhile Academy child health activity. At our October meeting in Boston, progress will undoubtedly be made along these lines by discussion of the suggested duties of National and State Committees, Regional and State Chairmen, etc., and how to bring about more active participation of every Fellow in some useful child health project of the Academy.

Chairman Stringfield, of Connecticut, with the aid of Program Chairman Grover Powers and an able committee of the entire Connecticut Fellowship (with Yale University cooperating) held a Regional Meeting in March, at New Haven, that was outstanding in its attendance, good fellowship, and pediatric educational values. The scientific program was splendid, and the symposium on various phases of adolescence was especially well presented.

The health problems of refugee children from Europe (entering this country largely through ports in Region I) have been extremely well handled by Dr. Stimson and his Committee.

Educating our states and provinces (adults as well as children) in nutrition is a challenge to our Academy for the year to come, as are the many peculiar health problems of children whose homes are in or near some of the numerous military or industrial developments connected with national defense. These problems are multiplying rapidly in Region I and will need our best thought and devotion to the cause of child health in the year that lies ahead.

All reports and data indicate that our Fellows in Region I, in addition to steadily improving the care of individual children in their private practices, continue to contribute a great deal of time, thought, and effort to the general needs of child health in their various communities, states, and provinces. This should be a matter of great pride to every one of us who is privileged to be a Fellow of the American Academy of Pediatrics.

Condensed Brief Statements of Province and State Activities in Region I:

In our Canadian Provinces of Quebec and Ontario, **Chairmen Goldbloom and Tisdall** and their Fellows are doing a great deal of excellent work along the line of nutrition and refugee children, as well as Child Health work connected with military defense.

In Quebec the Academy members have established a center for the examination of domestic employees. Under the leadership of Dr. Paul Letondal of the Department of Pediatrics, University of Montreal, a summer course in pediatrics, lasting over a period of two weeks, has been given at l'Hopital de la Misericorde. The course was known as "Le cours de perfectionnement en pediatrie." This enables the French physicians to have modern pediatric instruction in their own language. Dr. Albert Guilbeault has been conducting a city-wide experiment with B C G both by oral administration and intracutaneous injection. With one or two exceptions practically all eligible pediatricians in the Province of Quebec have been enrolled as Fellows of the Academy.

In Ontario **Province Chairman Tisdall,** as Chairman of the Committee on Nutrition of the Canadian Medical Association, developed an outstanding nutritional program for all Canada.

In Maine the members of the Academy, under the leadership of Dr. Fred Webster, have carried forward their good child health program in connection with local, state

and national health bureaus, with the addition in 1941 of the establishment of a cardiac clinic in Portland (federally financed by the Children's Bureau) and a thorough physical examination of boys and girls under the National Youth Administration.

New Hampshire, under the leadership of **Chairman Franklin Rogers,** has continued to carry on its well-rounded child health program and has formed a new State Pediatric Society of twenty-eight members, did special work on the Health Supervision of the 18,000 children in summer camps, gave radio talks on child health, and developed nutrition programs for defense, cooperating with the National Nutrition Conference.

Vermont's program, under the guidance of **State Chairman Paul Clark,** continues to be well-rounded, with expansion of the program in several directions. A state-wide child health meeting was held, with an attendance of over 400. A special nutrition program is being developed.

Massachusetts, with **State Chairman Sisson and Associate Regional Chairman, Lewis Webb Hill,** has continued to help guide the New England Pediatric Society in general child health developments in New England, as well as continuing the promotion of the excellent working relationship between the Academy and State Medical Society, and governmental, social health, and welfare agencies on behalf of expanding child health programs. Special programs on premature babies, care of rheumatic fever, and national defense measures have been developed. The Camp Committee, under the Massachusetts Department of Public Health, has published an important pamphlet entitled, "The Camping Number" of the State Department publication, "The Common Health." This publication is now available to professional and nonprofessional groups interested in the camp health problem.

The Rhode Island Fellowship, under the guidance of **Chairman Henry Utter,** has continued its past splendid program, and, in addition, has given lectures on vitamins in childhood, has forwarded the Crippled Children's program for cardiac children, has developed a premature infant care system, and has stimulated the routine use of Vitamin K to all newborn babies in the various hospitals of this state.

The Connecticut Fellowship, with **Chairman Oliver Stringfield,** besides acting as hosts for the splendid Regional Meeting, has continued its excellent Child Health program in connection with the State Board of Health and the State Medical Society, has developed a "Nutrition for National Defense" program, and is helping draw up health recommendations for emergency child care centers in industrial localities doing defense work.

Northern New York State, under **Chairman Beaven,** has continued its excellent educational program for rural practitioners and its good committee work on contact infections, child health relations, nonmedical groups, and school health.

Southern New York State, under **Chairman Alexander T. Martin,** has continued to integrate its large Fellowship in the very numerous Child Health activities of Metropolitan New York and vicinity, and in addition has (1) aided in the State Nutrition program, as part of national defense; (2) aided in the development of state program for care of children with rheumatic fever and heart disease, with a ninety-six-bed hospital at West Haverstraw and an educational program for physicians throughout the State; (3) made considerable progress in the setting up of standards for Mothers' Milk Bureaus; (4) taken an important part in the setting up of standards for hospital and home care of premature infants.

The New Jersey Academy, under **State Chairman LeRoy Wilkes,** has continued its well-integrated program with the State and County Medical Societies, State Department of Health, and State Health and Welfare agencies, and in addition, has outlined definite suggestions, at the request of the State Defense Council, for the evacuation of the children of New Jersey. This latter will be available in Boston, for interested Fellows from other seaboard States with a similar problem.

Our Pennsylvania Academy, under **State Chairmen Julian Lyon and E. R. McCluskey,** in addition to preparing to entertain the Regional Meeting in April, 1942, in Philadelphia, has steadily improved all former phases of the Academy program in cordial relationship with the new state governmental, health, and welfare agencies. Child Health Relations, contact infections, school health, and milk problems have received special attention. The committee on cooperation with nonmedical groups has developed a unique "Going to School Health Meetings" set of programs for mothers and interested groups. Camp health has also received special consideration.

Delaware, with **State Chairman Margaret Handy,** in addition to its previous child health program, has improved the work in tuberculosis testing, developed a nutritional and contact infection program, established a convalescent home for

cardiac and rheumatic children, and cooperated with the Alfred DuPont Foundation for Crippled Children.

Maryland, under **Chairman Fred Smith,** and under Chairman Knox of the Child Health Relations Committee, of the State Department of Health, has continued its excellent program of former years, with considerable expansion in necessary fields.

District of Columbia, with **Chairman H. H. Donnally,** has continued its numerous activities, with special activity on contact infections; helped promote a general meeting of 500 persons interested in infant and child welfare; took part in the National Nutrition Conference in May, 1941, where Dr. Joseph Wall was made Chairman of the important subcommittee on Nutrition of the National Defense Committee; and assisted in a three-day postgraduate session on Heart Disease held by the District of Columbia Medical Society and the Medical School of George Washington University.

From these reports, it will be seen that Region I and its states and provinces show a healthy rate of growth during the past year in the steadily expanding program on behalf of child health made necessary by present-day international, national, state, and local situations. [This will be further implemented by the forthcoming Boston discussions as to increasing the effectiveness of participation by our Fellows at state and community levels.]

We Fellows of Region I face the important Child Health Year that lies before us with utter confidence in the willingness of our splendid Fellows to shoulder all child health responsibilities necessary for our national defense and for the preservation of true democracy and the American way of life.

Respectfully submitted,

STANLEY NICHOLS
Regional Chairman

Report of Region II

The increase in the membership of Region II during the past year has been very satisfactory, but the attendance of the regional meeting this year at Richmond, Virginia, and last year at Biloxi, Mississippi, was not. The main reason for this is due to the tremendous area covered by Region II. Members in West Texas would have to travel about 2500 miles to reach the Memphis meeting. There is quite a demand among the Southern Pediatricians to combine the annual Regional Meeting of Region II with the Pediatric Section of the Southern Medical Association. Have called the meeting of all State Chairmen to meet at Boston for the purpose of trying to solve this problem.

Respectfully submitted,

HUGH LESLIE MOORE
Regional Chairman

Reports of State Chairmen of Region II:

GEORGIA.—During the past year we have had two meetings of the Georgia members of the Academy. The attendance has been excellent. We plan to have meetings every year in December and April. At the last meeting, we had a report of the chairmen of the various state committees.

The Committee on Child Health Relations is also the Committee from the Georgia State Medical Society as Advisory Committee to the State Health Department. Their work has been chiefly on educational lines. They assisted in the preparation of such pamphlets as the State Manual of Immunological Procedure. They were active in assisting the establishment of maternal and child health clinics throughout the state. Incidentally, there are 286 such clinics so established. They have cooperated in the devising and distributing of some 200 incubators throughout the counties of the state. They are working in every way trying to correlate the recommendations of the National Child Health Committee with our State Health Department's program.

The Committee on Contact Infection reported that they were following the recommendations of the National Committee as to tuberculosis. They suggested that servants and all adults who are in contact with children should be examined for possible infection, recommending routine tuberculin tests on all children, especially those under 3 years of age. They plan to have articles published in the State Medical Journal informing the medical profession of the recommendations of this committee. They are also developing an educational program through the State Board of Health for all the counties.

A report was also made of the progress of the Committee on Camping. The Chairmen of the other Committees made their reports, merely stating, "Progress is being made."

The members endorsed the attitude of the Academy to offer our services to the Surgeon General in any capacity in the field of National Defense.

The State Chairman for Georgia was asked to service on the State Nutrition Committee.

There were three new members added to the Academy in Georgia this year.

Respectfully submitted,

WILLIAM L. FUNKHOUSER
State Chairman

KENTUCKY.—This has been a busy year and much has been accomplished by the members of the Academy in holding special pediatric meetings, clinics, and conferences in strategic points in the state. There has been a carefully planned publicity campaign for each of these meetings. The doctors in the counties adjoining the meeting place have been contacted and there has been publicity given in the newspapers, and through the cooperation of the County Health Officer and the Parent-Teacher Association large numbers of children have been examined. Popular addresses have been made before the Parent-Teacher Associations and Women's Clubs, and when possible, also to one of the luncheon clubs. A number of such meetings were held with the cooperation of an obstetrician. These meetings were very greatly appreciated by the doctors.

Special effort has been made this year to secure more thorough medical supervision in the work of the Crippled Children's Commission of the State. As far as practicable, members of the Academy have been appointed on the visiting staffs of the hospitals doing orthopedic work. The pediatricians and internists doing the medical work have been put on salary and there is a little closer checkup of the children from the viewpoint of the pediatrician. A pediatrician also has made an examination of the children who have come to the orthopedic clinics throughout the state. In this way, a great number of cases of juvenile tuberculosis and also malnutrition and even serious blood dyscrasias have been checked up and treatment instituted.

Through the offices of the Sloan Foundation, a number of schools in the mountain districts of the state are being thoroughly studied to evaluate the nutritional needs of the children and to plan for the betterment of the children through special educational efforts.

The State Chairman is a member of the State Committee on Nutrition for National Defense and he has taken part in a great number of meetings and conferences throughout the state, planning for a better understanding and utilization of the modern knowledge of nutrition.

We have completed the ninth year of our special postgraduate course in pediatrics held at our Children's Free Hospital with the largest number of doctors in attendance at this meeting. The annual one-day meeting of the members of the Academy on the first day of the meeting of the State Medical Association has also grown in interest and attendance.

The members of the Academy have been most cooperative in all of these efforts and have most willingly given their time and abilities to any plans that have been proposed for the betterment of the children in our state.

Respectfully submitted,

PHILIP F. BARBOUR
State Chairman

OKLAHOMA.—Members, 11.

Committees—

1. Committee on Contact Infections
   Chairman: Dr. Anna Luvern Hayes, Tulsa
   Dr. C. E. Bradley, Tulsa
2. Committee on Child Health Relations
   Chairman: Dr. George H. Garrison, Oklahoma City
   Dr. A. L. Solomon, Oklahoma City
3. Committee on Cooperation with Non-Medical Groups
   Chairman: Dr. Ben H. Nicholson, Oklahoma City
   Dr. J. B. Snow, Oklahoma City
4. Committee on School Health
   Chairman: Dr. Hugh C. Graham, Tulsa
   Dr. Killis C. Reese, Tulsa

5. Committee on Camps
Chairman: Dr. Clark H. Hall, Oklahoma City
Dr. W. M. Taylor, Oklahoma City

There has continued to be very little activity of the Academy as an organization in this state, but the various members have been working in cooperation with existing organizations and groups. We have a small membership consisting of a group in each of the cities of Tulsa and Oklahoma City, and there has not been much opportunity for carrying out any organized program.

During the past year some of our members were called upon to furnish a total of four hours of teaching in each of three postgraduate courses in Obstetrics and Allied Subjects given through the Department of Obstetrics of the University of Oklahoma. The enrollment for each course was limited to four physicians whose qualifications were acceptable to the University. Each course was of two weeks' duration and organized on highly practical lines.

A postgraduate course in Pediatrics, sponsored jointly by the State Medical Association, the State Health Department, and the Commonwealth Fund of New York, has been in progress in the state since Feb. 12, 1940, and will continue till Jan. 31, 1942. Dr. James G. Hughes is giving the lectures. Up to now eight circuits have been covered, with a total of forty teaching centers. There has been a total enrollment of 725 physicians.

The Oklahoma Commission for Crippled Children has been carrying on a program for taking care of cardiac diseases since April 1, 1940. The work is done by members of the Academy. A weekly clinic is held at the Crippled Children's Hospital and to date 72 clinics have been held with a total of 584 visits. Four itinerant clinics have been held in different parts of the state with a total of 52 patients examined. Two hundred and ninety patients have been accepted on the Cardiac Program. Eight beds are available for these cases in the Crippled Children's Hospital and there are eight beds for convalescent and boarding home care.

The State Health Department is carrying out a very excellent maternal and infant welfare program which extends to various parts of the state.

Even though there is not much organized activity, I believe our members in this state are thoroughly conscious of the importance to them of such an organization as the American Academy of Pediatrics.

Respectfully submitted,

CARROLL M. POUNDERS
State Chairman

MISSISSIPPI.—Members, 10.

The members of the Mississippi State Pediatric Society are all very active and very much interested in the pediatric work necessary to bring about better health conditions in the children of this state. All of them respond very readily to any call for pediatric service, such as physical examinations of school children, children in orphanages, junior auxiliaries, and others who are unable to pay for such services. Many of us are called upon to deliver talks before Parent-Teacher organizations and other state and national programs, looking toward child welfare.

It has been the custom of the Mississippi State Board of Health, the Commonwealth Fund, and Tulane University to promote and conduct postgraduate lecture courses throughout the state every year. In these the pediatric service has been well represented by outstanding pediatricians.

The Mississippi State Pediatric Society has an annual meeting each year on the Monday afternoon and night before the meeting of the Mississippi State Medical Association, at which time we have out-of-state speakers and guests as well as our own state pediatricians to participate in the programs. The meeting was held this year in Biloxi on Monday, May 12, at which time we had a very fine attendance and a splendid program. The program of the meeting was as follows:

Round Table Discussions, 2:00 P.M.

Immunization in Contagious Diseases
Chairman: R. E. Wilson
Assistants: Byron Alexander
E. W. Bulley
Harvey F. Garrison, Jr.

The Newborn Period: Asphyxia, Infant Feeding, and Infections
Chairman: Harvey F. Garrison
Assistants: Guy Jarratt, Lamar Arrington
Guy Verner

Sulfanilamide and the Allied Drugs in Pediatrics

Chairman: N. C. Womack

Assistants: Van C. Temple
Charles Ward
F. G. Riley
C. E. Roach

Refreshment Hour, 5:30 to 6:00 P.M.
Banquet, 6:30 P.M.
Sulfanylguanidine in the Treatment of Bacillary Dysentery. George M. Lyon, Huntington, West Virginia

The medical profession as a whole was cordially invited to attend these meetings.

In addition to our annual meeting each year, the State Pediatric Society has other call meetings to attend to such business as may come before the society as well as discuss the general problems of the pediatrician.

There is always a very fine spirit of congeniality and cooperation among the members of our society and the members of the state medical association. Both associations work harmoniously to promote better health for the medically indigent as well as other children of our state.

At our state meeting this year, the members voted unanimously, favoring joint meetings of Region II with the Section on Pediatrics of the Southern Medical Association each year and urging that plans be adopted to bring about this kind of meeting. The present State Chairman was unanimously recommended as State Chairman for another term after the expiration of his present term.

Respectfully submitted,

HARVEY F. GARRISON
State Chairman

TENNESSEE.—In Tennessee we, as members of the Academy, continue to follow the policy of exerting our efforts through established facilities and agencies concerned with the restoration and promotion of child health. While this policy does not give any particular indentity to the Academy as such, still for our section of the country, it seems to offer the best methods of accomplishing the results for which we are all striving. And, while progress might be somewhat slower, more enduring results, based on a sound educational foundation for all concerned, we feel can be accomplished in this way.

A postgraduate course conducted by a good out-of-state pediatrician and covering all sections of the state over a period of two years was finished last January. This course was sponsored by the State Medical Association, the State Department of Health, and the medical schools, with aid from the Commonwealth Fund. Each summer an intensive course of one month is given at one of the medical schools. Other less intensive postgraduate work in pediatrics is given to doctors and nurses. Also, every opportunity is taken advantage of to aid in school health work, to help parent-teacher groups, tuberculosis organizations, the American Legion, and in fact, all groups and agencies, official and nonofficial, concerned with or interested in child health. The greater part of this cooperative effort is carried out by members of the Academy as part of their contribution to the promotion of child health. There are many specific examples of this cooperative effort which we shall not try to enumerate or describe.

There is much room for improvement, and that forms the theme of our purpose as we go along.

Respectfully submitted,

HORTON CASPARIS
ARTHUR G. JACOBS
Co-Chairmen

TEXAS.—There is a very close relationship between the Fellows and Texas Pediatric Society. Many active Committeemen are the same for both groups. Through their combined efforts, we have been able to have a pediatric program before the entire Texas Medical Society. We feel that this is a great step forward since it brings pediatric problems before the general practitioner whereas before they have been given only in our sectional meetings. Most of the activities of the Academy have been educational, the Fellows serving on many state-wide committees. Satisfactory progress has been made in the Summer Round-Up with the help of the Parent-Teacher Association and the State Health Department. Throughout

the entire state, the Fellows have cooperated in giving medical care to children of indigent World War veterans. Not one cent has been requested from American Legion funds for medical care within the 254 counties of Texas. A full-time pediatrician will act as a consultant for the Crippled Children Division and will help direct the work throughout the state, so that a complete examination and appraisal of the physical and mental condition of the child will be determined before any operative procedure is decided upon. It is the plan to have the pediatrician and orthopedist working together on each case. Much has been done to further development of Mental Hygiene Clinics throughout Texas. Dr. Southerland, of the University of Texas, is very sympathetic with the movement and we hope to have established soon at the University a Mental Hygiene Clinic.

Much progress has been made in child placement of dependent and neglected children. The Director of the Division of Maternal and Child Health of the State Department of Health is a member of the American Academy of Pediatrics, and through his efforts we are getting very close cooperation with the Department of Education and other Allied groups. We have formed a Texas interprofessional Commission on Child Development that offers much for Texas children.

Respectfully submitted,

B. J. BERGER
T. J. MCELHENNEY
Co-Chairmen

VIRGINIA.—The work in connection with the meeting of Region II in Richmond, on April 24 and 25, was the chief concern of the Virginia members during the past year. Despite the excellent papers presented on the program of this meeting, the attendance was discouragingly small.

In view of the meeting in Richmond of Region II, the usual spring clinical meeting of the Virginia Pediatric Society was not held.

In the field of child health and welfare, the outstanding event of the present year is the study of Child Welfare in Virginia now being made by the Virginia Legislative Advisory Council through its Child Welfare Committee. Because of the size of the task, it is probable that this study will be continued through another biennium. Through the work of this committee, it is hoped that important revisions in the scope and financial support of Child Welfare in the state will result.

Representatives from the Child Welfare Committee of the Medical Society of Virginia, including two members of the Academy, met last summer with the above legislative subcommittee on Child Welfare to discuss the outstanding needs as seen by this group. The following topics were discussed and recommendations made by the representatives of the Child Welfare Committee of the Medical Society of Virginia:

1. The present state of Mental Hygiene with the recommendation that as a beginning, three Mental Hygiene Clinics be established, mainly for diagnostic, but also for therapeutic work.
2. Extension of the benefits of full-time health units to all the counties of the state. At present only forty-seven counties comprising 68 per cent of the rural population are served by these full-time health units.

The committee feels that the creation of county health units in all the counties of the state constitutes a most important health measure for maternal and child welfare.

3. Additional appropriations for the use of the Commission for the Blind.
4. Department of Health control over sectarian and nonsectarian schools.
5. X-ray examination of all teachers in the primary schools of the state.
6. Extension and improvement of educational and other facilities of the industrial and normal training schools.
7. Expansion of facilities for the care of the feeble-minded and epileptics.
8. Provision of additional funds for educational work among the physically and mentally handicapped children.
9. Additional beds for the care of colored crippled children and for tuberculous children, white and colored.
10. Employment of a full-time pediatrist and one or more full-time nutritionists on the staff of the State Department of Health, to promote respectively the establishment and operation of well-baby clinics, and educational work in the field of nutrition.

During the past year, Dr. A. L. Carson of the Bureau of Maternal and Child Health, has established a Premature Station and Training Center at Lynchburg, Va. A member of the Academy, Dr. E. A. Harper, is in charge of the service. Besides the local service, two-month courses of intensive training in the care of

premature infants is offered to pediatric nurses from other hospitals throughout the state. The courses include both practical experience and didactic teaching.

The new Virginia Maternity Hospital Law became effective Jan. 1, 1941, and sets forth specific requirements for the care of maternity patients and newborn infants in hospitals, maternity homes, and other institutions. There has already occurred a rise in standards and continued improvement is expected. The infant death rate in the state, though still high, has shown a gratifying fall from 74 per 1000 live births in 1936 to 60.1 in 1940.

The Child Welfare Committee (mostly composed of Academy members) of the Medical Society of Virginia is urging a more general use of Sauer's pertussis vaccine; and the use of two or more doses of diphtheria toxoid (rather than the single dose method of inoculation that has been in current use by many physicians) and a subsequent Schick test.

In May, 1940, under the direction of Dr. E. C. Harper, head of the state Crippled Children's Bureau, there was organized a department for research in rheumatic fever and cardiac disease in children. This group, which includes a pediatrician and a cardiologist, has been doing some very effective work and has uncovered a number of cases of rheumatic fever with unsuspected heart disease. Provision has been made for hospitalization of these cases, where indicated, as well as subsequent observation and follow-up care. At present, only a limited portion of the state has been included in this work, but extension of the activity is expected.

The committee has also been endeavoring to arouse greater interest in the so-called "illegitimate" group of children in the state, to the end that the stigma of "illegitimacy" may not adversely affect their future as citizens. It is thought that better reporting of such cases and more careful placing in foster or institutional homes may prevent much of the unhappiness that sometimes follows such individuals through life.

Respectfully submitted,

JAMES B. STONE
State Chairman

WEST VIRGINIA.—The Academy in West Virginia has been active in many ways during the past year. The membership is being consulted whenever pediatric problems arise and several of the men are participating actively in various lay and professional organizations in the state.

On March 30, at Charleston, a called meeting of the membership was held with all except two of the members in attendance. Several topics were discussed: (1) Participation in a State White House Conference; (2) School Health Problems; (3) Revision of Communicable Disease Control Regulations; (4) Health Supervision in Summer Camps; (5) Regional Meetings.

Full discussion of these problems led to a resolution requesting the West Virginia State Medical Association to assume leadership in a Child Health Conference, if such a conference is held. The State Medical Association was also requested to ask for a revision of the State Regulations of Communicable Disease Control. In addition, the State Health Department was requested to make a health survey of all the summer camps for boys and girls.

The Academy is also represented on the State Nutrition Committee, and Dr. Raymond M. Sloan has recently been appointed liaison officer to the American Legion.

No member of the West Virginia Academy has been called into active military service although some are on the reserve list.

Respectfully submitted,

J. LEWIS BLANTON
State Chairman

LOUISIANA.—The thirteenth annual session of the Louisiana State Pediatric Society met at Shreveport on April 21, 1941, with Dr. H. Aubrey White, President, in the chair. The program committee, under the chairmanship of Dr. C. H. Webb, divided the program into an afternoon and an evening session; the first dealing with case reports and two papers on the newborn. One of these was on Resuscitation of the Newborn, by Dr. J. D. Russ, and the other on Epidemic Diarrhea of the Newborn, by Drs. Harvey Colvin and Mayo Emory, guests of the Society. The evening session followed a barbecue on Cross Lake, and was addressed by the President, Dr. H. Aubrey White, on the relationship of the pediatrician and his work in the rapidly increasing population of a military center, such as Alexandria, whose population has tripled within a period of six months. The officers elected for the

coming year at this meeting were Dr. Don Julian Graubarth, President; Dr. W. B. Worley, Vice-President; and Dr. W. C. Rivenbark was re-elected Secretary and Treasurer for a third term.

Dr. Charles McKhann was the guest speaker on pediatrics for the meeting of the New Orleans Graduate Medical Assembly, which convened from March 3 to 6, 1941.

Two members of the Academy in New Orleans have gone on active duty. Colonel Robert A. Strong was ordered to active duty as of April 4, 1941, and is attached as Medical Officer of the Third Military Area of the Fourth Corps. This area comprises the states of Louisiana, Mississippi, and Alabama. Dr. Sims A. Chapman was ordered to active duty in the Navy, with the rank of Lieutenant Commander, M.C., U.S.N., and is stationed at the United States Naval Air Station, Corpus Christi, Texas.

Recently, Dr. Paul Herron, of Oak Ridge, met his death in a most unusual manner. He was electrocuted while using an x-ray machine.

An addition to the pediatricians of the State of Louisiana is Dr. Chester A. Stewart, of Minneapolis, who has been appointed Head of the Department of Pediatrics at the Louisiana State University Medical Center.

Respectfully submitted,

JULIAN GRAUBARTH
State Chairman

Report of Region III

Region III reports with regret the loss by death of three of its members during the year:

Dr. A. Graeme Mitchell, Cincinnati, Ohio
Dr. Fred Moore, Des Moines, Iowa
Dr. Charles A. Wilson, Detroit, Mich.

Four Fellows have moved to other Regions:

Dr. Oscar N. Torian, Indianapolis (Sewanee, Tenn.)
Dr. Benjamin W. Carey, Detroit (Pearl River, N. Y.)
Dr. Chester A. Stewart, Minneapolis (New Orleans, La.)
Dr. Hart E. Van Riper, Madison, Wis. (Washington, D. C.)

One member has moved into Region III: Dr. Susan Page Souther, formerly with the Health Department of Hartford, Connecticut, is now with the Health Department of Columbus, Ohio.

Thirty-two new members have been added during the past year, making a total membership in Region III 412 as of September 1, when this report was prepared.

The last Annual Meeting of Region III of the American Academy of Pediatrics was held at the Palmer House on May 15, 16, and 17, 1941. The registration totaled 664, made up as follows:

Members	240
Nonmembers	214
Scientific exhibitors	8
Commercial exhibitors	87
Ladies	115

There were thirty-eight exhibit spaces occupied by thirty-four commercial exhibitors and ten spaces devoted to scientific exhibits.

At the luncheon meeting on Thursday, May 15, honoring Drs. Isaac Abt, Joseph Brennemann, and Thomas B. Cooley, there were 311 persons present.

The cocktail party and banquet Friday evening were attended by 403 persons.

One hundred and fifteen ladies attended the complimentary luncheon and style show at Marshall Field & Company, as guests of the Region.

After thorough discussion it was decided to continue the Committee on Arrangements in full charge of the annual meeting of the Region. The plan has functioned efficiently and provides for a continuing committee to handle the regional meetings.

Moved by Dr. Wiley Jones and seconded by Dr. George Munns, that the present treasurer continue to handle the funds of the Region for the ensuing year. The motion was passed unanimously.

The treasurer was empowered to arrange for an annual audit of the regional funds as of July 1, 1941, by a certified public accountant, the expense of the auditing to be paid from the funds of the Region.

The Committee on Arrangements for the next annual meeting was appointed as follows:

Dr. E. A. Wishropp, Chairman
Dr. W. J. Scott
Dr. W. S. Nolting
Dr. J. Hugh Lewis
Dr. Edgar E. Martmer, Ex Officio

Cleveland, Ohio, was selected for the next Annual Meeting of the Region, the time of the meeting to be decided by the Committee on Arrangements.

Dr. Henry Gerstenberger was appointed Local Chairman of the Program Committee and Dr. John Toomey, Local Chairman on Arrangements.

The policy of charging a registration fee sufficient to cover the cost of a luncheon and banquet ticket was discussed and the policy of charging a $5.00 registration fee was officially approved.

Reports of State Chairmen of Region III:

No reports received from Indiana and Iowa.

COLORADO: WILLIAM WILEY JONES.—I regret to report that the Academy has not been able to function as efficiently in Colorado as it is doing in many other states. This is due to several reasons.

Colorado is a very sparsely settled state covering a very large area. Of the fifteen Academy members, all but three live in Denver. There is no Pediatric Section of the State Medical Society. The Public Health activities of the state are carried out most efficiently by the State Board of Health. Under a competent full-time pediatrician, the Division of Crippled Children and the Division of Maternal and Child Health provide opportunities for diagnosis and treatment for all indigent children in the state who are affected with crippling conditions. They also maintain various prenatal and postnatal clinics and twelve well-baby clinics in the state. County public nurses have been assigned to thirty units within the state. A full-time specially trained epidemiologist is available to the communities and counties of the state. Special immunization clinics are conducted each year and all immunization biologics are furnished by the state. The division of tuberculosis control is under a full-time specialist who conducts throughout the state the tuberculosis finding clinic. Academy members have been appointed to all Public Health Committees by the President of the State Medical Society.

All members of the Academy are deeply interested as individuals in cooperating with the above work, but unfortunately because of distances involved, expense, and time, we do not see how the Academy members can be more active throughout the state. Also, we have learned that in many of the smaller communities, the local men resent the "outsider," feeling that they desire to do the work themselves under the guidance of the Division heads.

Your Chairman will receive with gratitude any suggestions that you may recommend as to making the work of the Academy in Colorado far more active than it is.

ILLINOIS: GEORGE F. MUNNS.—This report was published in full in the July issue of THE JOURNAL OF PEDIATRICS on page 141. Its main items may be summarized as follows:

A booklet on preventive pediatrics has been prepared, published, and is now being distributed to all physicians in Illinois by the State Health Department.

The Contact Infection Committee has been active and has succeeded in establishing a system of yearly examinations of school teachers and domestic servants in several communities in the state.

The Committee on Mental Hygiene and Aid to the Mentally Handicapped Child has been actively engaged in the development of state programs for educable mentally handicapped children and for mental health.

Recommendations have been made by the Pediatric Subcommittee to the Advisory Committee of the Commission for Handicapped Children relative to the pediatricians being present for pediatric examinations at orthopedic clinics now being held in the state.

A Coordinating Committee on Child Health for the State of Illinois has been organized. Fifteen different organizations interested in child health programs are represented on this committee which also includes five members of the Academy. Dr. Clifford Grulee is Chairman and Dr. Rollin Cutts, Secretary. This ought to be a very valuable accomplishment. More should be reported concerning it later.

KANSAS: PAUL C. CARSON.—Different members of the Academy are on the Maternal and Child Welfare Committees in the state. Assistance was given in a

tuberculin testing program for school children last spring. Dr. Carson is now formally associated with the State Society for Crippled Children as the pediatric consultant.

MICHIGAN: WYMAN C. C. COLE.—An active year for the Academy in Michigan. Personnel of Child Welfare Committee of the State Society identical with that of Academy's State Committee on Relations with Nonmedical Groups. Very advantageous arrangement. Outstanding piece of work accomplished—preparation of new law governing care of crippled and afflicted children in which pediatrician and not surgeon is the physician in control of all cases. The committee has also (1) developed a program for better care of premature infants in rural areas and small towns; (2) provided for a "Pediatric Coordinator" who travels through rural areas for educational and consultation purposes; (3) conducted refresher courses in various parts of the State; (4) enlisted whole personnel of the Academy as official consultants in poliomyelitis, with pay from public funds.

Seventy registrants were present for annual three-day postgraduate course in pediatrics.

Cited as the most important accomplishment of the year is the drawing up of a set of regulations of minimum standards for newborn nurseries. Plans have been sent to Dr. Clifford's committee for criticism and modification. [We hope that they may be presented before the Academy as a whole for approval at Boston meeting.]

MINNESOTA: ROGER L. J. KENNEDY.—Membership in the Academy is held by twenty-seven of the forty-one pediatricians in the state who have been certified by the American Board of Pediatrics. One application for membership is in the hands of the Regional Chairman.

The Committee on Cooperation with Nonmedical Groups, consisting of Dr. L. F. Richdorf, Chairman, and Dr. D. Siperstein and Dr. R. Nutting, report that they have interested the medical societies in sponsoring the showing of the movie, "When Bobby Goes to School" at the Annual Child Legion School, at ten P.T.A. meetings, to school nurses, and a continuous showing at the State Medical Society meeting in St. Paul. Other contacts were made with the American Legion, P.T.A., and the Board of Education through the medical societies.

Committee on Contact Infections: Dr. P. F. Dwan and Dr. E. S. Platou. The most important activity relative to the work of this committee is the unique program which was started in Meeker County. This program provides for application of the tuberculin test to the entire population in that county to be performed by the local physician, and, for making roentgenograms of the chest of each positive reactor. The Minnesota Public Health Association is assisting the program by providing publicity of educational nature and the State Medical Association has offered their services in the compilation of records. The State Association has also provided some financial support. Up to a recent date, 5,000 tuberculin tests have been completed on a group of children and adults, with a preponderance of children. Fourteen per cent reacted posiitvely. Roentgenograms have been made on 660 positive reactors and have resulted in the discovery of seven with parenchymal lesions. Three of these cases have been completely examined and have been sent to a sanatorium for treatment, whereas, the remaining four are still being studied. A second thousand paper films have just been ordered. The work is being done by the physicians in private practice in Meeker County, who examine and test the patients in their private offices and use local facilities for x-ray studies.

The Committee on Child Health Relations: Dr. C. O. Kohlbry, Chairman, Dr. E. D. Anderson, and Dr. E. F. Robb report that during the latter part of 1940 a new Committee of Child Health was formed by the Minnesota State Medical Association. The entire committee structure of the State Medical Association was changed so that specific committees will have specific interests and tasks. The State Chairman of the Academy is also Chairman of the State Committee on Child Health and, Ex Officio, a member of the State Committee on Public Health Relations. This, to date, has proved to be a very satisfactory arrangement.

Committee on Mental Hygiene: Dr. H. M. Keith, Chairman. Dr. Keith is also President of the Minnesota Mental Hygiene Society. This society was formed in 1939 and has been trying to lay a foundation for future work, particularly with a view to cooperation between the Medical Societies and State Department of Mental Hygiene and the various lay groups about the University and throughout the state. The University Psychiatric Center for Children is unquestionably the most active in the state as far as children's work is concerned. This is under the able direction of Dr. Eric Clark, assisted by Dr. Jenson. Another center has been the Mental Hygiene Clinic in Duluth. This has been under the partial direction of Dr. Gowan, a member of the State Medical Society who is also a member of the Board of the Mental Hygiene Society.

The chief activities of the Mental Hygiene Society have been general meetings to promote interest in the subject, appointment of committees to study the various activities which might be undertaken, cooperation with the Judge of the Juvenile Court, and recommendations to the legislature about State Hospitals. It is felt that the influence of the Academy could be of great benefit to the Mental Hygiene Society in the study of mental health and the Academy, itself, would probably benefit also through the cooperation of the groups interested in the Society's work.

In view of the great interest in nutrition at the present time, plans are being made by the State Child Health Committee for a meeting to discuss this subject in the near future. A representative from the Academy will be appointed to serve on the State Committee on Nutrition which is headed by Miss Inez Hobart, Extension Nutritionist, University Farm, St. Paul.

It has not appeared feasible to call a meeting of the State Academy members. They are practically all members of the Northwestern Pediatric Society which has been in existence for nearly thirty years and which serves as an admirable clearing house for pediatric matters.

Just recently, the Bureau for Crippled Children of the State Department of Social Security has arranged for the examination by pediatricians of the state who have been certified by the American Board of Pediatrics of all children attending the Crippled Children's Clinics.

The Chairman would urge that so far as possible, at every regional and national meeting, more time be allowed for the meeting of the State Committees and other members of the state organizations in conjunction with the various national committees. He feels that if such arrangements were made, the members of the state organizations would return to their respective states imbued with considerable enthusiasm as well as with a more specific objective.

MISSOURI: PARK J. WHITE.—Co-Chairman Dwyer has done a vast amount of work on behalf of project for pediatric supervision of crippled children and inclusion of cardiac children in this category.

Several Academy members are taking active interest in "interracial pediatrics," starting with clinics and scientific meetings led and attended by both negro and white physicians.

The Contact Infection Committee for Missouri is accomplishing its purposes mainly through the St. Louis Pediatric Society and the Tuberculosis and Health Society of St. Louis, acting together. Success for the program for domestic help is recorded, but the same project for school teachers has encountered difficulties.

The St. Louis Children's Hospital is setting an example for other hospitals by its plan (in operation) for preliminary and periodic examination of staff and employees.

NEBRASKA: JOSEPH A. HENSKE.—All certified pediatricians in the state are members of the Academy. Members of the Academy serve on practically all committees in local and state organizations that have anything to do with education, preventive measures, child welfare, etc.

Academy members meet during the year and act as an Advisory Committee on pediatric problems that come up from time to time, such as the M.C.H. Program, etc. We have found that this method of discussing various problems with the organizations has not only improved the efficacy of the pediatric care of the children in the state, but by open discussion of the various problems, made for better understanding between the pediatricians and organizations and a more smoothly running organization. In Nebraska, all of the members except two, who are located in Lincoln, reside in Omaha, and through our Nebraska Pediatric Society which meets every month, except during the summer, we hold a free discussion of all pediatric problems with the members who are not eligible for certification. We have had splendid cooperation with our local and state societies.

NORTH DAKOTA: RALPH E. PRAY.—Members 4.

Academy programs accomplished through Committee for Maternal and Child Care, representing the State Medical Association. Activities under way: (1) State-wide program for better premature care. Dr. Pray spent two months touring the state in the interests of this program. Reports definite success; (2) Program for care of cardiac cripples in formative stage, but prospects good that it will be launched in full swing before long; (3) Cooperation with Children's Bureau and state orthopedists in Crippled Children program. Subordinate position to orthopedists regretted. Slowly working toward correction of situation; (4) Moving picture, "When Bobby Goes to School," shown freely in Fargo. Plans for rest of state under way; (5) Participation in American Legion's Child Health Program.

OHIO: STERLING H. ASHMUN.—Eighty Academy members in state widely spread out. Accomplishments largely through individual members, but sum total of accomplishments reflected in consistent improvement in the attitude toward contact infection, lessening of maternal and infant morbidity and mortality, lessening in diphtheria and smallpox, and an improved cooperative spirit in the whole field of child health and welfare.

1. Thirty Academy members are teaching in the Medical Schools of Ohio in Cleveland, Columbus, and Cincinnati.
2. Eighteen have taken part in the postgraduate lectures conducted by the State Medical Society in the Five-Year Plan of regional lectures.
3. Thirteen or more are school examiners, eleven are scout examiners, and nine are camp examiners.
4. Three counties have committees on Contact Infection. Many others have plans for such a committee.
5. Three members still serve on Certified Milk Commissions. (Note by Dr. Ashmun: "Why we still have certified milk, I do not know.")
6. Fifty-eight or more have from one to eight clinic positions in Ohio hospitals.
7. Thirty-six teach in Nurses' Training Schools.
8. Fifteen have spoken to nonmedical groups.
9. Eighteen members have participated in county society programs.
10. Two Academy members serve on the State Medical Society's Committee on Education.
11. Dr. Ashmun is Vice-Chairman of the Committee on Postgraduate Lectures.

Care of the cardiac cripple has just begun in Ohio. Major activity in this field in prospect. Academy members expected to be represented on Board for Care of Crippled Children in near future.

The following tribute to the memory of Dr. Mitchell comes from the Ohio group:

"The whole Academy realizes the loss that we have suffered, especially in Ohio, in the death of our Director, teacher and leader, A. Graeme Mitchell, but I am sure that no monument can do more to honor him than every member's rededicating himself to the highest ideals of Pediatric practice, and to make every effort to embody that fine spirit of professional conduct that made Dr. Mitchell the ideal for all of us who knew him. He was never worried about the demand for pediatric service, but he was always desirous that our services should represent the very best that we could offer. His respirations have ceased, but his aspirations will live forever."

SOUTH DAKOTA: GOLDIE ZIMMERMAN.—Maternal and Child Welfare Committee appointed at last State Medical Meeting. Academy program carried out through this Committee.

Film, "When Bobby Goes to School," has been shown widely and received favorable comment.

WISCONSIN: A. B. SCHWARTZ.—Outstanding gain in past year in Child Welfare work in Wisconsin has been discernible willingness of various groups to work together. (1) Shown by greater cooperative effort between Parent-Teacher and medical groups; (2) White House Conference Child Health continuation program has named Academy members as Chairmen; (3) Through special committees, Academy members have helped direct programs in Child Welfare towards goals set by the national meetings.

Child-placing agencies have begun to discard classification "unadoptable." Better teacher training in child health instituted. Over eighty incubators available for premature infants born in rural areas. Program of whooping cough vaccine administration being initiated in Milwaukee.

SASKATCHEWAN, CANADA.—Saskatchewan has but five pediatricians and three doing pediatrics exclusively. Province Chairman, John S. Brown, only member of the Academy. The Academy is becoming much better known and will, I hope, include more members from this Province in the not-too-distant future.

Child welfare has not as yet suffered any serious setback as a consequence of a vigorous war effort. This work is much more efficient in the cities with all-time school physicians who are pediatricians or who have had special training for this work. [Well-Baby Clinics, with a pediatrician supervising under the Health Department of the city concerned; are doing considerable work for good.]

Rural areas are reached by visiting Clinics, examining and spreading Federal Bureau of Health brochures suited to the occasion, or apparent needs of the community visited. This work is under the control of the Provincial Board of Health, acting in accord with the Federal Department of Health and with due consideration

of the advice and council of the Provincial or District Society. At this time, we have an epidemic of encephalitis lethargica, encephalomyelitis and poliomyelitis threatening us, which called forth universal effort to subdue and this appears at the moment to have been successful.

It is my impression with the small membership in the Academy here, best results at present could come only through effort in and through the District and Provincial Medical Organizations. I hope with an increase in representation and with cooperative effort to show more and better results.

Thus the report of Region III indicates the growing significance of the Academy as an organization devoted to the interests of the children of America. It is indicated, first, by the constantly increasing membership list; second, by an outstanding successful annual meeting attended by better than half the Fellows; and, third, by the reports of the State Chairmen which clearly show a truly marvelous spirit of individual and collective effort at raising the standards of health among children.

Respectfully submitted,

LEE FORREST HILL
Acting Regional Chairman

Report of Region IV

The good "old Spanish custom" of furnishing an annual regional report has been faithfully attempted. Letters were written to the several state chairmen of the Region, and in true "Spanish style" reports were submitted by five of the twelve states in this Region. It may be presumed that this absence of further reports is due to the fact that the others had no report to offer, that August is the universal month for pediatric vacation, or that they are suffering from the disease "mañana."

Dr. Frank H. Douglass, of Washington, reports cordial relationship with the various health agencies of the state and the inauguration of a new idea: The presentation of a pediatric problem under the title of "Clinical Forum" in each issue of *Northwest Medicine*.

From Wyoming, Dr. Paul W. Emerson, the sole Academy member of the state, reports that he took part as the pediatrician in the first Child Welfare Conference held in the state. He is a member of the State Committee on Nutrition and has made his contact with the American Legion. He is also on the committee of the county medical society members, cooperating with a Public Health Unit about to be formed.

Reporting for Arizona, Dr. Vivian Tappan states there are four Academy members. Because of its larger membership (fourteen) Academy projects are referred to the Arizona Pediatric Society for action. Through this indirect sponsorship, the Academy exercises its influence on (1) Well-Baby clinics, (2) pediatric examination and pediatric care of children admitted to the "Crippled Children's Service," (3) pediatric care of all children in public medical institutions, (4) cooperative plans with nonmedical groups and societies, and (5) the handling and supervision of "Contact Infections." Several other projects are under way for the improvement of pediatric care of the children of the state.

From southern California, Dr. Victor E. Stork reports that the local members again are sponsoring through the Southwest Pediatric Society, their annual two-day clinical session with Dr. Horton Casparis as the honored guest. He feels that a noteworthy impetus to the tone of pediatric work in the community has been contributed by the appointment of Dr. Joseph Brennemann as Chief of Staff of the Children's Hospital of Los Angeles and as head of the Pediatric Department of the University of Southern California.

Dr. M. K. Wylder, of New Mexico, reports five Academy members in the state. Each is active on some committee. They have had several radio broadcasts on pediatric subjects. Dr. Wylder, as a member of the State Board of Health, has been successful in guiding the activities of this group in the pediatric field.

The annual regional meeting was held in San Francisco in May, 1941. Attendance at regional meetings has steadily increased and this meeting had the largest registration to date.

In addition to a scientific program of the highest order, a business meeting was held which developed some points of more than passing interest.

The regional membership authorized the chairman to address the following letter to (1) the Surgeon General of the United States Army; (2) the Surgeon General of the United States Navy; (3) the Chairman of the National Defense Program:

"Whereas pediatricians are eager to serve in the National Defense Program to the best interest of the Federal Government, and

"Whereas the pediatrician occupies an unusually favorable position, by virtue of his training and experience, with regard to the management of nutritional problems and the problems concerned with sanitation and contagious disease control, therefore

"Be it resolved by Region IV of the American Academy of Pediatrics in session in San Francisco, California, May 1, 2 and 3, 1941, that the Surgeon General of the United States Army be respectfully urged to outline the objectives to be fulfilled in the Army by the pediatricians of the nation individually and collectively, and that furthermore

"In the formulation of such a policy for the service, both public and private, of pediatricians to the nation, that their exceptional training in nutritional problems, the care of the contagious diseases, and the supervision of child welfare in the nation be given especial consideration."

Satisfactory replies were received from Mr. McNutt through Helen S. Mitchell, Director of Nutrition; Surgeon General James C. Magee (Army) through Brigadier General Love, Medical Department Assistant; and Rear Admiral Ross T. McIntire, Surgeon General of the United States Navy. The replies may be summarized by saying that the request will be followed by these departments insofar as it is practicable to do so.

Other business of especial importance was the appropriation of $500.00 from surplus regional funds for the purpose of purchasing sulfanilamide and sulfathiazole to be sent to the British Pediatric Society for use in the care of the children of Great Britain. The details in connection with the expenditure of this money and the arrangements for the shipment of the drugs were handled by Dr. Norman K. Nixon.

Through the cooperation and generosity of the Lederle Laboratories this $500.00 made possible the sending of 200,000 5 gr. sulfanilamide tablets and 26,000 ½ Gm. sulfathiazole tablets, quantities greatly in excess of those obtainable at the usual professional discount prices. The sulfanilamide tablets were sent in two separate packages, one on each of two ships especially designated by the British War Relief and the American Red Cross following clearance through the United States State Department. The sulfathiazole tablets were shipped on four bomber planes direct from Los Angeles to Canada and from there to England via Newfoundland.

Letters of appreciation of this gift have been received from Charles McNeil, President; Arthur Maitland-Jones, Honorary Secretary; and W. G. Wyllie, London Representative of the British Pediatric Society. The depth of feeling expressed by the letters from these various men was a source of great satisfaction to the members of Region IV, and the hope is expressed that other regions may find it possible to do similarly should funds be available. Through the British Ministry of Health, Dr. Maitland-Jones was able to arrange the distribution so that every Children's Hospital in Great Britain received a certain proportion of the tablets, which he said were difficult to obtain.

Arrangements are now being made for the next regional meeting which will be held in Los Angeles in April or May of 1942.

Respectfully submitted,

EDWARD B. SHAW
Regional Chairman

Reports of Committees

No reports from the following:

Committee on Honorary Fellows
Committee on Immunization and Therapeutic Procedures
Committee on Medical Education
Graduate Education
Undergraduate Education
Committee on Camps
Committee on Vitamins
Council for Pediatric Research

Report of the Committee on Central and South American Scholarships:

Since the American Academy of Pediatrics established the Committee on Central and South American Scholarships in November, 1939, this Committee has approached several University Foundations and large industrial concerns who have generously granted seven scholarships for Central and South American pediatricians. The grantors are: The Procter Foundation of the University of Cincinnati, the Mayo Foundation, Mead Johnson & Company, Abbott Laboratories, Quaker Oats Company, M & R Dietetic Laboratories, and the Wisconsin Alumni Research Foundation. These scholarships consist of $1,200 a year and most of them are available for three years.

The following universities and hospitals have expressed their willingness to take the candidates: Johns Hopkins University, Harvard University, University of Chicago, University of Minnesota, Chicago Children's Hospital, University of Cincinnati, Mayo Clinic, University of Iowa, Western Reserve University, Yale University, University of Illinois, University of Wisconsin, Vanderbilt University, University of California, University of Rochester, and the University of Pennsylvania.

As soon as these scholarships had been procured, the Committee approached the national pediatric societies of the following countries: Cuba, Mexico, Chile, Brazil, Uruguay, Argentina, and Venezuela. It was suggested that each national pediatric society appoint a committee which would take charge of the selection of the most suitable candidate, and the following committees on Central and South American Scholarships have been appointed:

Mexico

President: Dr. Enrique Baz-Dresch

Members: Dr. Jesús Lozoya
Dr. Roberto L. Sanchez

Annual Secretary of the Mexican Society of Pediatrics: Dr. Luis Berlanga Berumen

Cuba

President: Prof. Angel A. Aballí, Professor of Pediatrics at the University of Habana

Members: Prof. Clemente Inclan, Professor of Experimental Pathology at the University of Habana
Prof. Agustin Castellanos, Assistant Professor of Pediatrics
Prof. Teodosio Valledor, Assistant Professor of Pediatrics

Secretary: Dr. Serafín Falcón, Secretary of the Cuban Society of Pediatrics

Advisor: Dr. Henry P. Carr, Rockefeller Foundation

Argentina

President: Dr. Ramon R. Arana, Director of the Children's Hospital of Buenos Aires and Actual President of the Argentine Pediatric Society

Members: Prof. Mamerto Acuña, Bs. As., Professor of Pediatrics
Prof. Pedro de Elizalde, Bs. As., Professor of Pediatrics
Prof. Raúl Cibils Aguirre, Bs. As., Director of Public Assistance
Dr. Fernando Schweitzer, Professor of Pediatrics in La Plata

General Secretary of the Argentine Pediatric Society: Dr. Alfredo E. Larguía

Chile

Dr. Gonzalo Moraga Fuenzalida, Ex-President of the Chilean Pediatric Society
Dr. Adalberto Steeger
Dr. Manuel Muñoz, Vice-President of the Chilean Pediatric Society
Dr. Agustin Inostrosa, President of the Chilean Society of Pediatrics
Dr. Joaquín Luco, Representative of the Guggenheim Foundation

Venezuela

Dr. Pastor Oropeza, Director of the Venezuelan Archives on Child Health and Pediatrics
Dr. Gustavo H. Machado, Ex-President of the Venezuelan Society on Child Health and Pediatrics
Dr. Espíritu Santos Mendoza, Chief of the Division on Maternal and Child Health of the Ministry of Hygiene and Public Health
Dr. Ernesto Vizcarrondo, Actual President of the Venezuelan Society on Child Health and Pediatrics

Uruguay

President: Dr. Conrado Pelfort

Members: Professor Dr. José Bonaba
Professor Dr. Victor Zerbino

Brazil

Prof. Pinheiro Cintra, Prof. Cath. of Pediatrics of the Medical School of the São Paulo University

Prof. G. H. Paula Souza, Prof. Cath. of Hygiene, and Director of the Hygiene Institute of the São Paulo University

Prof. Pedro de Alcantara, Prof. Cath. of Pediatrics, of the Paulistan Medical School

Dr. Octavio Gonzaga, Director of the Institute of Puericulture of the State Health Department, indicated by the General Director of the P.H.D. of the State

Dr. Jorge de Queiroz Moraes, as representative of the pediatricians of the Medical and Surgical Society of São Paulo, indicated by the President of this Society, Prof. Franklim de Moura Campos.

Dr. Mario da Silva Margarido, Ex-President of the Section on Pediatrics of the São Paulo Association of Medicine, and Dean of the pediatricians of São Paulo.

Prof. J. E. Santos Abreu, President of the Section on Pediatrics of the São Paulo Association of Medicine

Up to the present time, Dr. Fernando Madero G., of Mexico, Dr. Julio Meneghello, of Chile, and Dr. Gustavo Cardelle Penichet, of Cuba, have been appointed. Dr. Madero is using the scholarship granted by the Abbott Laboratories and has begun his work at the Bobs Roberts Memorial Hospital in Chicago; Dr. Meneghello recently arrived in the United States and is planning to work at Harvard University (scholarship of Mead Johnson & Company); Dr. Cardelle will use the scholarship contributed by M & R Dietetic Laboratories.

It is to be hoped that a number of the scholars may be present at the meeting of the American Academy of Pediatrics in Boston.

Respectfully submitted,

HENRY F. HELMHOLZ, Chairman
SAMUEL Z. LEVINE
FREDERIC W. SCHLUTZ
FRANCIS SCOTT SMYTH

Report of the Committee on Contact Infections:

The organization of this Committee reaches into every state. Most of the larger communities have Academy members as representatives on the State Committees. However, in a few states which one would expect to be the most progressive, the Committee is small and inactive.

Reports have been received showing very encouraging progress with the campaign for examination of nursemaids and houseworkers for proof of freedom from tuberculosis and other infections which might be transmitted to children. New York City, Buffalo, Troy, N. Y., Westchester County, N. Y., St. Louis, suburbs of Chicago, Washington, D. C., and several other cities have recently been very active in this direction.

The American School Health Association has been in close touch with this Committee. There is a mutual desire for our Committee and theirs to cooperate, in order to increase the number and efficiency of health examinations of school teachers for the exclusion of those who have active tuberculosis.

In Westchester County, New York, all practicing physicians have been urged to make use of the tuberculin test routinely on their private adult patients who are associates of children. The radiologists in that county have agreed to take single film lung x-rays at a low fee for all who show a positive tuberculin reaction.

Discussion at the round table on Tuberculosis during the annual meeting may bring out points which can be applied by the pediatrician toward providing a more completely tuberculosis-free environment for children under his supervision.

All members of our state committees have recently been circularized with a letter giving a summary of the progress which has been made with our program in various cities. It is hoped this will act as an incentive and guide for those which have been less successful in their efforts and accomplishment.

Respectfully submitted,

FAIRFAX HALL, Chairman
GAYLORD W. GRAVES
REGINALD A. HIGGONS
CHESTER A. STEWART
PARK J. WHITE

Report of the Committee on Cooperation With the American Legion:

As this is the first report of this Committee, a general survey of the subject was deemed essential.

American Legion.—The American Legion, considered together with its official organizations, the Auxiliary, the Forty and Eight and the Eight and Forty, has a

combined membership extending up into the millions. Every town and section of the United States is represented. The Legion, also, is a cross section of American life. It is also the greatest peace organization existing in America at the present time.

The American Legion has a Department of Child Welfare which is thoroughly organized. It has a permanent full-time personnel, the Chief of the Division being Miss Emma Puschner assisted by Mr. Milton Campbell and Mrs. Seibert. This Child Welfare Department is divided into areas, states, and local groups. Its purpose is to assist the existing established organization in raising better future generations of Americans. The Legion has a sinking fund to take care of the children of indigent legionnaires. The Legion has under its control a large number of publications, local and national in scope, as well as access to the radio.

Specific Child Welfare Activities.—These Child Welfare activities may be considered under three headings: Legislation, Subsidation, and Education. The present time is a time of emergency and cooperation may be extremely valuable. Whether we have war or not, there will be a period of reconstruction where such cooperation will be necessary.

Legislation: There is a large amount of legislation that will be necessary; also, there will be even a larger amount which for various reasons should be defeated. The Legion has shown a willingness to advise with the Academy and to act in unison. It can readily be seen the amount of influence that can be brought to bear on Legislation through this organization.

Subsidizing: The Legion is willing to cooperate with the Academy, although the sinking fund is to be used for the children of legionnaires. Raising funds in other manner could be jointly agreed on by the two organizations.

Education: In education, particularly, could these two organizations work together with benefit, taking as our basis that the American home is the center of all activity for the greatest mass of people in our country. Education must begin here, extending through the home and parents of the child. The parents should be particularly educated as to certain types of activities as immunization for various types of infections, etc. Educate the mother, and the family physician will fall in line. The similarity of organization between the Legion and the Academy will here be manifest. The Auxiliary, particularly, will provide the audiences and allow members of the Academy to reach the home. This activity will interest many physicians who have not previously been interested in Child Welfare. Specifically, it will get many of the legionnaires and potential legionnaires to see that the Legion has really an interest in this subject.

Recommendations of This Committee.—First, that the Academy express to the Legion its willingness to cooperate; that its interest is in the betterment of the American child; that we wish, as pediatricians, to be used in the best way possible in this emergency; that we are willing with them to cooperate with other acceptable organizations in every way possible; that this can best be accomplished by an organization, together with the Legion, of the areas, states, and local groups, realizing that each locality has its particular problem.

What Has Been Done.—The Legion, through its officials, has indicated that it is willing to cooperate with our program fully along these lines. Each State Chairman has been requested to appoint a chairman in each state to act in liaison with a representative appointed from the Legion; these two to fully organize a local program and to appoint necessary committees. These state and local groups are to work with the area and national groups. It is felt by this Committee that the program will develop itself when so organized.

In closing, the Executive Board felt that a special committee was necessary for the purpose of full cooperation. Members of the Executive Board who were legionnaires were appointed to this Committee because it was necessary to meet at least twice a year, and it was felt in this way that extra expense to the Academy could be avoided. It is now felt that a new Committee should be appointed.

Respectfully submitted,

EDWARD C. MITCHELL, Chairman CLIFFORD G. GRULEE
HUGH K. BERKLEY STANLEY NICHOLS

Report of the Committee on Cooperation With Nonmedical Groups:

The activities of this Committee remain confined to its cooperative program with the National Congress of Parents and Teachers in an effort to increase the number and improve the quality of health examinations of children.

The Committee's contribution to this joint program has been (1) participation in producing the sound motion picture film, "When Bobby Goes to School," (2) preparation of a brochure supplementing the film entitled, "Health Appraisal of the School-Aged Child: Minimum Standards," and (3) preparation of a short paper

describing the production and purposes of the film intended for the use of physicians who wish it in introducing showings of the film before lay audiences. In addition, it should be stated that the National Congress of Parents and Teachers has prepared a pamphlet for distribution to members of lay audiences who view the film.

At its meeting in Chicago on June 1, the Executive Board of the Academy approved the Committee's two publications and voted that they be printed for distribution to physicians without cost. Mead Johnson & Company again kindly consented to assume responsibility for their publication and distribution. Mead Johnson & Company is also publishing the pamphlet of the Parent-Teacher Congress.

Thus the preliminary organizational program envisaged by the Academy's Committee and the National Congress of Parents and Teachers as being most suitable for obtaining results in its educational drive has been completed. Now when the film goes out to a medical audience, a certain number of copies of the brochure will accompany it. If there is an insufficient number of copies, additional ones may be had by individual physicians writing directly to Mead Johnson & Company. When the film is to be seen by a lay audience, the article describing its purposes will accompany the film for the introducing physician's use, as will also the pamphlets of the Parent-Teacher Congress for distribution among the audience.

Pending the completion of the above phases of its program, the National Committee has been relatively inactive in attempting to create interest and activity among its state subcommittees. This is the immediate task ahead. While a great deal has already been accomplished in many states by Academy members cooperating with local Parent-Teacher groups, it is the Committee's feeling that a great deal more can be accomplished. It is planned to make this phase of the Committee's work the basis for discussion at the meeting with State Subcommittee Chairmen in Boston in October.

Respectfully submitted,

LEE FORREST HILL, Chairman	WARREN SISSON
DENNIS H. KELLY, Secretary	C. A. ALDRICH
ALBERT D. KAISER	JAMES W. BRUCE
MARGARET NICHOLSON	JOS. A. JOHNSTON

Report of the Committee on the Fetus and the Newborn Infant:

In April, 1939, a joint meeting of committees representing the American Committee on Maternal Welfare, the American Pediatric Society, and the American Academy of Pediatrics found ample evidence that fetal and neonatal mortality could be materially reduced through a widespread application of present knowledge. This joint committee felt that the members of the American Academy of Pediatrics could promote interest in bringing about improvement along certain clearly indicated lines if they could be provided with concrete recommendations that they could sponsor in their respective communities. The general subjects to which they felt attention could be directed were as follows:

1. Standard definition of terms
2. Revisions in the nomenclature of causes of death and in the list of acceptable diagnoses
3. Adoption of new stillbirth, birth, and death certificates, and recommendations as to their use
4. Need for more frequent and careful autopsies on stillbirths and neonatal deaths, and recommendations as to procedure
5. Hospital records and medical routines (physical examination of newborns, etc.), hospital statistics, analyses of records, staff conferences
6. Community studies of neonatal morbidity and mortality; reports and analyses; follow-up studies
7. Hospital regulations and licensure
8. Requirements for protection of neonates at different periods and under varying circumstances; standards for facilities and care
9. Means of securing widespread attention to recommendations

Your Committee accepts the foregoing as its long-term objective. We are at present working on standards for newborn nurseries. All of the State Chairmen have been circularized for information on this subject. At this time, we wish to extend our appreciation for their splendid response. We hope to have specific recommendations to offer by this time next year. We will welcome the suggestions of any member of the society.

Respectfully submitted,

STEWART H. CLIFFORD, Chairman	ARTHUR H. PARMELEE
LAURENCE R. DEBUYS	RALPH M. TYSON

Report of the Committee on Cooperation With Governmental and Medical Agencies:

The seven-point program of our Committee, now renamed the Committee on Cooperation With Governmental and Medical Agencies, which has for its objective "the making of each State Fellowship of the Academy the principal advisory group for the State Departments of Health and other official state agencies and the State Medical Societies," is continuing to make steady progress in most of our states.

Six complete additional state reports have been received, bringing the completely reporting states up to thirty-eight in number and encouraging progress reports from many states show commendable steps forward on one or more of the seven points in our program.

At the meeting of our National Committee at Memphis, in November, 1940, a seventh point was added to our program, as follows:

"Each Chairman of the State Child Health Relations Committee and the Committee shall endeavor, by every practical means, to stimulate increased responsibility for, and increased participation in, all types of Child Health service, in their own community, in their own County and State, by every State Fellow of the American Academy of Pediatrics."

This seventh point, when carried into effect, will be of great assistance to each State Chairman of the Academy in his efforts to promote Academy activities at State levels and make the Academy Fellowship in each State an increasingly important factor in all state Child Health developments.

The reports from the various states show clearly that, in addition to the utilization of the President of the American Academy of Pediatrics in the matter of offering the assistance of the Fellowship in each state to the State Medical Society and State Health and other public departments, it will be necessary, in some states at least, for the State Chairman of the Academy definitely to take part in this offer of aid and assistance by our Fellows to the Child Health programs of state, governmental, and medical agencies.

The Committee will endeavor at our Boston meeting to incorporate this idea into its seven-point program.

At the meeting of the State and National Committees in Boston, there will be general discussion of other suggestions, aimed at definite methods of making the seven-point program more effective, and presentations will be made by some of the State committees from states where the program has come into being most successfully.

Respectfully submitted,

STANLEY NICHOLS, Chairman	OSCAR REISS
MARTHA M. ELIOT	PHILIP F. BARBOUR
GEORGE M. LYON	PAUL W. BEAVEN
ALEXANDER T. MARTIN	W. L. CRAWFORD

Report of the Committee on Hospitals and Dispensaries:

A recent survey made of pediatric dental care in pediatric hospitals and outpatient dispensaries in this country and Canada, indicates that there is a very definite gap in the medical program for children due to unavailable and inadequate facilities for dental care in most communities.

This is a problem to which the American Academy of Pediatrics could very well give leadership and guidance in correcting.

Respectfully submitted,

GEORGE F. MUNNS, Chairman	MURRAY H. BASS
JOHN A. BIGLER, Secretary	LAURENCE R. DEBUYS

Report of the Committee on Legislation:

The only questions of moment coming to the attention of the Committee were the two bills relating to physical education, the first of which, H. R. 10606, was introduced by Mr. Schwert, October 3, 1940, and referred to the Committee on Education of the House.

This bill was so profoundly objectionable in many respects that it met with much opposition, and on the part of the Academy protests were especially made by Dr. Harold H. Mitchell, Chairman of the Committee on School Health, as well as President-elect Dr. Edward C. Mitchell, through the American Legion.

H. R. 10606 died a natural death at the expiration of the Seventy-Sixth Congress.

However, another bill was introduced on January 3 by Congressman Schwert with considerable change in its content, and again this was referred to the Committee on Education of the House.

The chairman of this committee was communicated with and a request made for the privilege of appearing in opposition if and when H. R. 1074 might be considered by this committee.

The title of the bill was markedly changed and the words, "health education" were left out, while in their place was inserted "guidance in healthful living."

Copies of the new bill were furnished to the President of the Academy, Dr. Richard M. Smith; Dr. Harold H. Mitchell, Chairman, Committee on School Health; Dr. Edward C. Mitchell, President-Elect; and Dr. Warren R. Sisson.

The new bill contains some ambiguous and questionable features.

Shortly after the introduction of this bill, Congressman Schwert died in Buffalo, N. Y., and whether or not this bill has a new sponsor we do not know.

We question whether the Congress will take up any such bill at the present time, but the committee has been asked to notify our President, Dr. Harold H. Mitchell, and the Chairman of the Committee on Legislation, should it be considered by them.

Copies of the two bills have been submitted to the Executive Board.

The Committee on Legislation would recommend that in the formulation of the manual for State Chairmen a clause be inserted to this effect:

"State Chairmen are asked to hold themselves in readiness to assist the Committee on Legislation in favoring or opposing, through their local representatives in Congress, any national legislation which has either a beneficent or harmful influence on pediatrics or pediatricians, when such aid may be requested by the Committee on Legislation."

Respectfully submitted,

JOSEPH S. WALL, Chairman
ISAAC A. ABT
JAY I. DURAND
PHILIP VAN INGEN
ALFRED A. WALKER

Report of the Committee on Medical Education (Postgraduate Education):

The Committee on Postgraduate Education has nothing to add to the report previously sent to the Executive Board except to recommend collaboration with the Associated State Postgraduate Committees on the same plane as the College of Surgeons and the College of Physicians, and this among other things will include a contribution of $50.00 for the year 1941-1942, check payable to Leroy E. Parkins, M.D., Treasurer, Associated State Postgraduate Committees.

One comment may be in order and that is that there has been a tendency to a falling interest accompanying the greater pressure from defense activities and dislocations therefrom. It has been more difficult to get clinical instructors this past summer. There is a growing interest in the attendance at short-term intramural refresher courses for the general men such as are being conducted at Saluda and in some of the University teaching centers.

Respectfully submitted,

GEORGE M. LYON, Chairman
HORTON CASPARIS
ADOLPH G. DESANCTIS
HUGH L. DWYER

Report of the Committee on Mental Health:

This Committee has felt that mental growth and development and the conditions influencing mental health are an important part of Pediatrics. If this statement is true, it naturally follows that the subject should be included in the pediatrics curricula of the medical schools. As a basis for discussion of this subject, the Mental Health Committee, with the cooperation of the Educational Committee, formulated a possible program of teaching last year and sent a copy of it to the Chiefs of the Pediatric Departments of the medical schools for criticism and comment (a copy is attached—"The Teaching of Mental Health in Medical Schools and Hospitals"). Replies were received from thirty-three schools. The following is a summary of these reports:

Thirty-two of the thirty-three schools were strongly in favor of the program in general. One-third of the schools did not think it was wise to begin the teaching of mental health before the junior year of medicine. All but five of the schools include specific courses and discussions on mental health in their Pediatric Departments. Of the five schools who do not have specific courses in mental health and development in their Pediatric Departments, two indicated that courses would be given this year. Some medical schools reported need for physicians especially trained in the problems of mental health. In this connection it might be recalled that scholarships are available for training of this kind. The number of teaching hours devoted to mental health varies from five to nineteen, the average being about twelve hours.

The Committee is gathering material for a motion picture on mental health in infancy. This picture is made possible by a grant from the Pet Milk Company. The scenario will be presented to all members of the Academy for suggestions and criticism within the next few months.

During the past year the Committee has received many helpful suggestions from members of the Academy. We hope many more will be received during the coming year.

Respectfully submitted,

BERT I. BEVERLY, Chairman	BRONSON CROTHERS
C. ANDERSON ALDRICH	GEORGE J. MOHR
FREDERICK H. ALLEN	ARTHUR H. PARMELEE
HORTON R. CASPARIS	VICTOR E. STORK

TEACHING OF MENTAL HEALTH IN MEDICAL SCHOOLS AND HOSPITALS

The Committee on Mental Health of the American Academy of Pediatrics would like to make the following comments regarding the teaching of Mental Hygiene in the medical schools and offer a program to be used as a basis for discussion of a plan for this teaching.

1. It is generally agreed that Pediatrics concerns itself with growth and development of children. This definition implies a consideration of those factors which stimulate an optimum growth and development of each child, the problems of child rearing, and the care and general supervision of sick and well children.

2. The teaching of all phases of the subject to medical students, interns, and residents enables them to grasp the problems of the whole child and the child as a whole.

3. In teaching the fundamental principles of normal growth or health of children, the intellectual and emotional as well as its physical phases are considered. In addition, medical students can learn to analyze and evaluate the effect of environmental factors on the mental and physical health of children.

4. Because of the integral relationship between physical and mental growth and the physiological influence of one upon the other, a consideration of mental health is an important part of every pediatric teaching program. This becomes more important when one realizes the importance of the first two years of life, which period is almost entirely under the care of a pediatrician or general practitioner of medicine. During the first part of life, physical and mental growth cannot be easily distinguished from one another; the same reactions have physiological and emotional attributes. Good physical hygiene is good mental hygiene and vice versa. Especially during infancy, mental health is dependent upon physical health and vice versa.

5. For these reasons, the Committee on Mental Health would like to suggest to the chiefs of the Pediatric Departments of medical schools and hospitals the following plan of teaching:

I. A short series of lectures to first-year medical students which will sensitize them, orient them, and open their eyes to the tremendous importance of this phase of child care and its relation to practical medical practice.

II. A course in growth and development in the Department of Pediatrics which would bring out the interrelationship of physical and mental health.

III. A course in the Pediatric Department covering habits, management of emotional difficulties, attitudes and techniques of parents, social adjustment, adolescence and the management of problems such as anorexia, enuresis, and school problems. This course should stress preventive technique. It should consider the signs of serious behavior problems in need of extreme psychiatric care.

IV. The mental hygiene aspect of the management of sick children should be integrated with bedside and clinic teaching. The well-baby clinic can be utilized to demonstrate normal growth and the psychologic as well as the physical care of normal babies.

V. It is felt that mental health can, partly at least, be taught by the pediatric staff or by those who speak and feel the pediatric idiom rather than by psychiatrists without pediatric training and experience. A pediatrician who has had training and experience in mental hygiene problems of children may be better able to present the subject to medical students than a psychiatrist who has not had extensive experience with children.

VI. A Mental Hygiene Clinic in the Pediatric Department has an invaluable influence on medical students and the pediatric staff. In this way, every one can observe psychiatric technique and follow his own cases which are largely lost if referred to another department.

VII. Machinery can be set up in pediatric wards and hospitals for teaching interns and house officers.

In proposing this program it is recognized that it is a matter for each school and hospital to work out a program in keeping with its facilities and methods of teaching.

Report of the Committee on Mothers' Milk Bureaus:

The purpose of this Committee, which was appointed one year ago, is to set uniform standards for the operation of all Mothers' Milk Bureaus in this country and in Canada, and which will be under the sponsorship of the Academy. Accordingly, in order to set the wheels in motion, a tentative draft of standards was sent out in July to the Advisory Committees of all the Bureaus in this country and in Canada, by Dr. Carl H. Laws, Secretary. These standards are those under which the Mothers' Milk Bureau of the Children's Welfare Federation of New York City is now operating, and have been used as a starting point for discussion. When replies have been received from the various Bureaus, these will be pooled and submitted to the Committee at the Annual Meeting in Boston for revision and recommendation. It is hoped that the Academy will not only sponsor the Mother's Milk Bureaus, but that it will also give certification to the Bureaus when they have met the standards which have been set by the Academy.

Respectfully submitted,

ALEXANDER T. MARTIN, Chairman	E. EARL MOODY
CARL H. LAWS, Secretary	WILLIAM J. ORR
JULIUS HESS	CLEMENT A. SMITH

Report of the Committee on National Defense:

Organized in the summer of 1940 as the Committee on National Defense and Relief and under the temporary Chairmanship of Dr. Borden Veeder, your Committee has gradually grown during the intervening year in number of members and in the scope of its activities. In the spring of 1941, its title was changed by the Executive Committee of the Academy, to the Committee on National Defense. At the present time, August 20, 1941, the field of action of the Committee lies in the following five directions.

1. Pediatric Care of Refugee Children Brought to America Under the Auspices of the United States Committee for the Care of European Children.

Over 700 English children were given careful physical examinations in the summer and autumn of 1940, and throughout the winter individual cases and small groups received some attention. In June, 1941, 110 Continental evacuees were examined and 45 more are due on Labor Day. Practically all of this work has been done in New York City, although known isolated instances of assistance have been given in other parts of the country and probably a great deal of pediatric care has been contributed to the United States Committee's widely scattered children of which we have no record. Dr. Rustin McIntosh is Chairman of this Subcommittee and his office has lists of Pediatric volunteers living in Manhattan, the Bronx, and neighboring districts. Dr. Carl Laws has similar lists for Brooklyn and Queens and has also spent a considerable amount of time in this activity. The services of thirty or forty different doctors have been used up to the present time.

2. Nutrition. A Subcommittee consisting of Drs. Katherine Bain, Allan Butler, Edwards Park, William H. Sebrell, and Joseph Wall as Chairman has been formed to cooperate with other agencies in the enormous task of improving the nutrition of the American people. Members of the Subcommittee, together with a number of other members of the general committee on National Defense and several officers of the Academy attended and participated in the National Conference on Nutrition held in Washington in May, 1941. Dr. Wall, on invitation from Dr. J. S. McLester, Chairman of the National Research Council's Subcommittee on Medical Nutrition, participated in a study, particularly of criteria for the recognition or suspicion of early deficiency states in children, adolescents and adults.

3. Cooperation with the Children's Bureau.

Dr. Martha Eliot having expressed a desire for young pediatricians who would take Civil Service Examinations and then help in the work of her bureau for the furtherance of child health, particularly in so-called "mushroom" communities that have sprung up in connection with war industries, Dr. Clifford Grulee has had compiled in his office very extensive lists of the pediatricians of the country, including Pediatric interns and residents, and young practitioners who have not yet become Diplomates of the American Board of Pediatrics. Copies of these lists

have been sent to Dr. Eliot, so that she can circularize the doctors with information about the needs of her bureau and possibilities for usefulness in that connection. The same lists were supplied by Dr. Stokes for use in activity No. 4.

4. Pediatrics in the Army. In the first World War, many of the pediatricians were used indiscriminately in the Army in all sorts of medico-military activities for which their specialized training was unsuited. It seems advisable to try to have pediatricians spared from being used as regimental Medical Officers, Hospital Supply Officers and the like, in the present emergency, but rather to keep them available to support civilian needs. Men especially trained in contagious diseases and in the field of nutrition could be of value to the armed forces. To cooperate with the Army in the provision of such men, a Subcommittee has been formed consisting of Drs. Robert A. Bier, Harry H. Donnally, Douglas D. Martin, and Joseph Wall with Joseph Stokes, Jr. as Chairman. A questionnaire has been sent to 2000 or more pediatricians, and information is being obtained of those who have had training and are available for service as diagnosticians attached to Army Hospitals. Some assurance has been received from Army authorities that men will be placed properly, and if at all possible they will be kept at fixed posts with a minimum of shifting.

5. Cooperation With Plans for Civilian Defense. The field of activity for the organized pediatricians of the country, in connection with possible mass evacuations and with disaster relief, has not yet been definitely worked out. Contacts have been made with Mayor LaGuardia's National Committee for Civilian Defense and particularly with the Director of Medical Activities therein, Dr. George Baehr, but there is nothing definite to report as of August 20. Certain communities, notably Boston, have gone ahead with local plans; and pediatricians, notably our President, Dr. Richard Smith, and Dr. Lendon Snedeker, have been very active in this work.

It is probable that there will be important developments in the activities of your Committee between now and the Boston meeting, an oral report of which can be given at the special meeting on National Defense which will be held Thursday evening, October ninth.

Respectfully submitted,

PHILIP M. STIMSON, Chairman
KATHERINE BAIN
ALLAN M. BUTLER
HARRY H. DONNALLY
CARL H. LAWS
DOUGLAS D. MARTIN
RUSTIN MCINTOSH
EDWARDS A. PARK
W. H. SEBRELL
LENDON SNEDEKER
JOSEPH STOKES, JR.
BORDEN S. VEEDER
JOSEPH S. WALL

Report of the Nominating Committee:

The Nominating Committee recommends the following nominations:
For President (President-Elect)
Dr. Borden S. Veeder, St. Louis, Missouri
For Regional Chairman (Region III)
Dr. Lee Forrest Hill, Des Moines, Iowa

(Signed)—Nominating Committee
DR. PHILIP M. STIMSON, Chairman
DR. VICTOR E. STORK
DR. ALFRED A. WALKER
DR. MATTHEW WINTERS

Report of the Committee on Nursing Education:

This Committee feels that there are three necessary essentials as regards the proper education of a girl in Pediatric Nursing.

1. Uniform minimum educational requirements in each state for entrance into Grade A Nurses' Training Schools such as two years of high school education, or better, a complete high school education.

2. Standardization of the medical content of the courses taught nurses in their undergraduate pediatric training.

3. Development of a standard graduate course in pediatric training for nurses.

This Committee has been working on the second and third requirements with two committees of the National League of Nursing: "The Committee on Nursing Education," and "The Subcommittee for the Study of Advanced Courses in Pediatric Nursing." Experimental courses have been evolved and are being offered in the School of Nursing Education of the Children's Hospital in Cincinnati. This Committee has advised particularly in respect to the medical content of these courses. The results have been very satisfactory. The Academy committee believes

that such courses should ultimately be adopted as the standard minimum by the National League of Nursing Education and the American Academy of Pediatrics, and also that each State should adopt these courses as their minimum standard requirements. The latter may be influenced by the joint action of Academy State Committees and State Nursing Associations.

The first requirement mentioned above, uniform minimum educational requirements in each state for entrance into Grade A Nurses' Training Schools, is being considered now by the Academy Committee and will be reported on later.

Respectfully submitted,

MERLIN L. COOPER, Chairman
STANLEY GIBSON
WILLIAM P. LUCAS
WILLIAM A. MULHERIN
CHARLES A. WEYMULLER

Report of the Committee on School Health:

ENCOURAGING TRENDS IN SCHOOL HEALTH

Our last report pointed out some common unsound policies and procedures of school health programs and recommended principles for the improvement of school medical service. New evidence that is accumulating indicates trends that are definitely encouraging and in accord with the recommendations of your Committee. The following are some of the tendencies noted in school health literature and to some extent in actual practice:

1. More emphasis is placed upon medical guidance and consultation than upon medical inspection or annual health examinations.
2. The limitations of a school health service are being recognized and the personal physician and other community medical facilities are being regarded as essential parts of health service to the child.
3. More attention is being given to medical history, to teacher observations, and to the quality of medical judgment which considers the whole child rather than adherence to frequent examinations and the stressing of the physical defects discovered.
4. Examinations by private physicians and dentists are being increased in some communities and fewer school authorities are assuming that they can meet all the needs for health supervision of the school child.
5. Screening devices such as observations of the teacher, sickness absence records, dental service records, Snellen and audiometer testing, and teacher-nurse conferences are used more and more for economical case finding and there is less preoccupation with the routine medical examinations.
6. Policies are being defined with long range planning by educational, public health, and medical leadership, and in some places there is evidence that "mutual appreciation of the other person's problems and clear definition of what each shall contribute to their solution" is replacing mere school or health authority.
7. A realization of the responsibility of parents for caring for their children seems to be making some gains over previous trends to provide all health supervision through the schools.
8. The objectives for the physician and nurse in the schools are being defined more and more in terms of health education, and there is a growing tendency to recognize that the purpose of the school health service is "to present information, to motivate to action, and to guide that action." Education for individual responsibility is more often mentioned than formerly, and there is less heard about complete and thorough health supervision through the schools.

These trends in thinking and the few actual changes in activity in school health programs offer new opportunities for medical leadership in this branch of public health. They are consistent with the principles of the American Medical Association and the best tradition of medicine.

The State School Health Committees of the American Academy of Pediatrics in Connecticut and Michigan have offered splendid examples of long range planning with reports on school health policies that have come from "mutual appreciation" of the problems of educators, public health workers, and the medical profession. The cooperative inquiry in Connecticut formed the basis of the report published in the *Journal of the American Medical Association* and *Hygeia*.[1] The Michigan report will be published by the State Department of Public Instruction at Lansing, Michigan, this fall.

Dr. Philip Van Ingen has given valuable pediatric leadership as Chairman of the Advisory Committee of the "Astoria School Health Study"[2] which should influence the thinking and lead to changes in practice throughout the country. This study has already caused far-reaching changes in our largest city. The "administrative research" methods used in analyzing the service and in making the changes point

the way for new developments in the future. The Report, which will soon be published, interprets all the changes which we have cited as new trends and suggests many other improvements in harmony with medical thinking that will have application throughout the country. Dr. Van Ingen has described these "new objectives" and "new and better practices" as aiming at "an effective utilization of organized effort for the better health of school children." In the opinion of the Chairman who has reviewed the preliminary text, it offers the best guide available for directing school health programs according to the philosophy expressed in the reports of this Committee and according to sound principles of education and medical service.

The trend towards medical guidance, consultation, and a more comprehensive understanding of the whole child through the sharing of information by all who work with him has been well expressed by Benjamin Spock, M.D., in "The Changing Task of the School Physician."[3] This series of articles appearing in *Progressive Education* gives a stimulating interpretation of what is meant by medical guidance and consultation and the possibilities of health supervision through the school without assuming responsibilities that are not the function of the school medical service.

As the work of the physician does not accomplish very much in the average public school situation without the assistance of the well-qualified nurse, it is worth while for pediatricians who would exert influence on school health practices to study the 1940 Report of the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association: "The Nurse in the School, an Interpretation."[4]

In interpreting new objectives and better practices to educational leaders, it is often useful to quote educational authorities. The chapter on the "Administration of the School Health Program" in "Social Services in the Schools,"[5] a Report of the Educational Policies Commission of the National Education Association, is such a report sanctioned by educational leaders and is valuable in presenting some of the newer trends.

The unique opportunity of pediatricians in State Committees, in medical schools, and as community leaders demands some familiarity with problems of organization and administration of school health work as well as recognition of those trends that seem desirable to physicians. An excellent discussion of these problems has been presented by John W. Studebaker, U. S. Commissioner of Education, and Fred Moore, M.D., late Director, Department of Health, Public Schools, Des Moines, Iowa.[6] They clearly set forth the educational function of all that is done for the health of the child. Commissioner Studebaker interprets organization principles and Dr. Moore gives an excellent explanation of the multiple relationships which need to be established in the adequate development of a school health program that is educational. They both insist upon only one form of organization and repeatedly assert the superiority of education department control until the reader must expect that unnecessary difficulties, duplications, and inefficiencies overwhelm all programs that are not under the complete control of the school authorities. This bulletin is based upon the experience of Dr. Moore in Des Moines and shows clearly how through organized effort the school can contribute to the teaching of "children and parents to be resourceful, self-reliant, and intelligent in meeting their own health problems." While the "purely service level" of a school health program has often been seen under health department control, the emphasis in Des Moines upon health education was unique and only a few other programs under education department control gave such an emphasis. There is undoubtedly a strong tendency for medically trained leaders to prefer to have the emphasis in the schools upon education rather than service. The important thing is to get strong medical leadership such as was given by Dr. Moore. Too often the educators employ physicians only for examinations and not for administration and leadership, so that some of the best medical direction has been given by health departments.

"Health Appraisal of the School-Aged Child, Minimum Standards,"[7] by the American Academy of Pediatrics Committee on Cooperation with Nonmedical Groups, and the motion picture, "When Bobby Goes to School," are recommended as valuable for promotion of sound medical service.

"School Health Services"[8] by W. Frank Walker, Dr. P. H. and Carolina R. Randolph is of interest because of the kind of activities in Tennessee that are described as typical of many programs both urban and rural. It is interesting to note that many of the conclusions and the recommendations of the study are in line with our recommendations, although the program described is characteristic of what we have criticized. There is a notable absence, however, of recognition that the private physician might make the examinations of some of the children although for periodic dental examinations the private or clinic dentist is recommended.

References

1. Suggested School Health Policies, American Medical Association, Chicago, Illinois.
2. The Astoria School Health Study. To be published.
3. The Changing Task of the School Physician, Benjamin Spock, M.D.; Progressive Education, 221 West 57th St., New York City.
4. The Nurse in the Schools, an Interpretation, Joint Committee on Health Problems in Education of the National Education Association and American Medical Association. National Education Association, 1201 16th St. N. W., Washington, D. C.
5. Social Services in the Schools, Educational Policies Commission of the National Education Association, 1201 16th St., N. W., Washington, D. C.
6. Organization and Administration of School Health Work, Fred Moore, M.D., and John Studebaker, Bulletin 1939, No. 12, Federal Security Agency, U. S. Office of Education, Washington, D. C.
7. Health Appraisal of the School-Aged Child, American Academy of Pediatrics.
8. School Health Services, Frank Walker, Dr. P. H., and Carolina R. Randolph, the Commonwealth Fund, 41 E. 57th St., New York.

Respectfully submitted,

HAROLD H. MITCHELL, Chairman	CLIFFORD D. SWEET
ROCKWELL M. KEMPTON	ARTHUR E. WADE
M. HINES ROBERTS	ESTELLA F. WARNER
A. CLEMENT SILVERMAN	LEROY A. WILKES

Report on Publicity:

This year, due to world conditions and the events of the war, the newspapers of this country have had a much greater volume of vital news than at any time in the past few years. Though there have been ever-increasing developments in the war and in our own national defense program, the American Academy of Pediatrics has received wide coverage.

Despite the fact that the press associations have cut their domestic coverage to a minimum, the two major news services carried thirteen stories devoted to Academy activities. Science Service, which supplies the larger newspapers with news of scientific developments, also carried four releases and two syndicate writers featured the Academy in their columns.

A total of 320 clippings have been received from our clipping services on the regional meetings. It has been found, however, that we can expect less than a 40 per cent return from the clipping services. Therefore, at least 650 Academy stories actually appeared in newspapers throughout the country.

The Region I meeting was covered from coast to coast and, in addition, Catherine Mackenzie, a writer for the Sunday Magazine Section of the *New York Times*, commented on it in one of her articles.

In a number of West Virginia papers, the Region II meeting was made the subject of editorials. This meeting was covered photographically as well as editorially.

The Associated Press carried a story released from the Region IV meeting nationally and a similar article appeared in *Newsweek*, a weekly news magazine.

Two child health writers, Gladys Huntington Bevans and Myrtle Meyer Eldred, devoted stories to the Region III meeting.

Aside from the newspaper and magazine publicity on the regional meetings, ten broadcasts were arranged during the meetings, making a total of two and one-half hours of free radio time. Eight talks were made by Academy Fellows over stations WMBG, WRNL, and WRVA in Richmond. On one of these talks, the station arranged with the Parent-Teacher Association to circularize all members of the Association in the state by post card to have them listen to the broadcast. The station manager later reported that he believed they had the highest listening audience they have ever had.

In San Francisco, KSFO and KPO also gave time to the problems of child health. The program on KPO, a fifteen-minute talk on Lowering Infant Mortality Rates by Dr. Norman K. Nixon, was carried nation-wide by the National Broadcasting Company. A number of other programs were carried on local chains and over state-wide associations of stations.

Besides the meetings, we have counseled with various members of the Academy who have written or telephoned the office. We have assisted in building up the convention mailings for the regional meetings and, in the case of two of the regions, had a number of meetings with the convention executives prior to the meetings.

All of the clippings received have been mounted and presented to the Secretary of the Academy.

Respectfully submitted,

LAWRENCE H. SELZ

Report of the Committee on Hospitals and Dispensaries:

IS PEDIATRIC DENTAL CARE AVAILABLE AND ADEQUATE?

Dental care is an important part of the child health program. In order to ascertain what the situation is in regard to pediatric dental care, a questionnaire was sent to pediatric outpatient departments and hospitals. Twenty-four of these questionnaires were returned in complete enough form for analysis. The following summary has been compiled from the available information.

I. Is pediatric dental service offered in connection with your outpatient department?

Twenty of the twenty-four clinics offer dental service in an organized dental clinic which has some close connection with the outpatient department. In only fourteen of these twenty clinics are all children in need of dental service referred to their own dental clinic for care. Unfortunately no inquiry was made as to how many of these children received dental care, or as to how adequate was the care that was given. Some interesting comments, however, were made voluntarily by those in charge of the clinics.

From one clinic came the statement that, "Due to the prevalence of dental disease only a comparatively small number of patients receiving general clinic treatment are able to be rendered adequate dental treatment."

From another clinic that offers dental service to all its patients comes the comment that, "The dental service offered to dispensary patients is quite limited. While any children in need of dental care are referred for it, only the most urgent needs are met and then quite inadequately, in the light of modern practice. Practically the only form of treatment is extraction. Perhaps 10 per cent of the children receive really adequate care."

Another clinic has ample facilities for dental care, but all children requiring dental care are not referred to it because of a matter of "internal organization."

The following comment came from a dental clinic where about 900 patients a month are rendered some service: "We all know all such clinics do little more than barely scratch the surface, no matter how large or how much work is done. However, I do feel that such services are of definite value."

From the foregoing comments it seems that although dental clinics may be a part of most outpatient departments to which all patients are referred, in many instances, at least, it is impossible to offer adequate dental service.

II. If there is a dental clinic in connection with the outpatient department, are all children in need of dental care referred to it?

In six of the twenty clinics that have a dental department not all of the clinic patients in need of dental care are referred to their dental clinic. This seemed to be due to the fact that facilities were not sufficient to care for all patients. In two clinics figures were not available as to the number of patients not accommodated. In one clinic 30 per cent and in another 75 per cent of the children could not be offered service in the dental clinic. In another clinic that had ample facilities referrals were made elsewhere because of a matter of internal organization. In one instance this part of the questionnaire was not answered.

When patients must be referred elsewhere for dental care, there is apparently little follow-up to see that the patients apply for and receive adequate dental care. This is important as experience in one clinic indicates that in that community adequate dental care is impossible to obtain for most patients.

III. No dental service offered.

Four of the twenty-four clinics offer no dental service. In these clinics the patients are referred to other agencies or are given a list of agencies to which they may apply for dental care. No follow-up as to whether dental service has been rendered is made except in isolated cases. Three of these outpatient departments do not have available space for a dental clinic, and in two of them it would not be possible to staff such a clinic.

IV. Orthodontic service.

Orthodontic service was offered in only eight clinics, and these also had dental departments. Twelve other clinics had dental departments but no orthodontic service was available. Neither orthodontic nor dental service was given in three clinics, while in one clinic without a dental department orthodontic service was available for postoperative oral surgery cases only.

The amount of orthodontic work done, when such was offered, varied greatly. In one clinic all cases were accepted, in another 80 per cent, in two 50 per cent,

in one 5 per cent, and in one only postoperative oral surgery cases. The two clinics that accepted most of the orthodontic cases were intimately connected with dental schools. No statements were made as to the number of patients accepted or the extent of the service performed.

In the fifteen clinics that do not offer orthodontic service, referrals are made to other agencies in ten, and in five nothing is done. When referrals are made to other agencies, the number that receive treatment varies. In one clinic all patients in need of orthodontic treatment were referred to the university dental school. The following estimates were given of the percentage of patients who received the required corrective work when referred to other agencies: Less than 10 per cent in two instances; 5 per cent; 3 per cent; 1 per cent; and one clinic thought it was questionable whether any received adequate, required corrective work.

V. Available dental care and the community.

Most of the clinics to which the questionnaire was sent are in large communities. Each clinic was asked whether there was any problem in obtaining dental care for the clinic type of child in the community which it served. Rather than give just a summary of the answers to this question, it is more enlightening to list the problem as it was said to exist in each community. Each state or city in the table represents a separate clinic in that community.

From the following summary of available dental care, it can readily be seen that in the majority of the communities such care is not available or adequate. Also the majority opinion is that a better dental program should be made available for

	Do you consider that provisions for needed pediatric dental care are adequate and available in your community for the clinic type of child?		Do you think a better program for dental and orthodontic care would be advisable for clinic patients?	
	Yes	No	Yes	No
Chicago		X	X	
Chicago		X	X	
Chicago		X	X	
Chicago		X		X
New York	X		Ours is adequate	
	Manhattan	Brooklyn		
New York	X	X		
New York		X	X	
Boston	X			
Boston		X	X	
Washington		X	X	
Pennsylvania		X	X	
Ohio		X	X	
Ohio		X	X	
Ohio		X	X	
California				X
California		X		
Wisconsin		X	X	
Indiana		X	X	
Iowa	X			X
Michigan	X			X
Maryland		X	X	
Missouri		X	X	
Canada	X			X
Canada	X			X

clinic children. In only four communities was it felt that adequate dental care was available for all children who need it. Two of these clinics were situated in moderate sized communities in midwestern states, and both had intimate connections with university dental schools. The other two clinics were both of those in Canada to which questionnaires were sent. This failure to provide for dental care in most communities seems a rather severe indictment of the care that is given children because dental care should be a part of a good medical program. From this summary it would seem that this part of the health program has been neglected.

Only a few of the clinics were able to give an estimate of the number of their patients who were in need of dental care but who did not receive it either in their clinic or in the community. In three clinics most of the children in need of dental care did not receive it, in one 90 per cent, in two 75 per cent, in one 50 per cent or more, and in one 33 per cent. This is certainly not a good showing when one considers that only those children registered in clinics are included in the above estimates. Here it is not a matter of family ignorance or failure to apply for care.

This absence of available and adequate dental care certainly should be made known if only that some movement for its correction will be initiated. That the problem is a real one becomes more evident when one considers the comments from many of the clinics. Such statements as the following were made:

"Due to the prevalence of dental disease, only a comparatively small number of patients receiving general clinic treatment are able to be rendered adequate dental treatment."

"We have a large number of children who are referred to and examined by a dentist, but because of lack of funds and limitations of space, it must be frankly admitted that the treatment given them is distinctly different from that which we and the dentists would recommend."

"I would say that the vast majority are not receiving dental care."

"Our outpatient dental clinic takes care of approximately 900 patients per month. In your above question as to the adequacy of the facilities I answered yes, but as we all know all such clinics do little more than scratch the surface, no matter how large or how much work is done. However, I do feel that such services are of definite value."

"There needs be a better educational staff and community program.".

"We have practically no provision in our community for dental care. This lack creates a serious gap in the medical program for the child."

Summary.—There seems to be a very definite gap in the medical program for the child due to unavailable and inadequate facilities for dental care in most communities surveyed. This is a problem to which the Academy of Pediatrics could very well give leadership and guidance in correcting.

Respectfully submitted,

GEORGE F. MUNNS, Chairman
JOHN A. BIGLER, Secretary
MURRAY H. BASS
LAURENCE R. DEBUYS

Report of Committee on Camps:

A formal report of the activities of the Committee on Camps was not rendered this year with the reports of the special committees of the Academy. It was felt that the accomplishments of the committee were somewhat difficult to assay and tabulate. A summary of the activities of the Committee on Camps since its inception has been composed which I hope can be published in the JOURNAL in the Academy Transactions.

There are a few problems which I should like to present to the Executive Committee for consideration and advice. Before doing this I should like to outline briefly what has been undertaken in the past year. Following the previous meeting, we met with the American Camping Association to assist in the "workshop" on camping, sponsored by the Kellogg Foundation. Dr. Henry Utter and Dr. Roger Kennedy, members of the committee, participated in this conference. They report most enthusiastically in regard to this round table, and there has been published an extensive report which gives suggestions and standards for medical supervision of camps. This year they have again asked us to be represented, but because their meeting coincides with the Academy meetings, no one of our committee will attend. We have, however, deputized Dr. Charles F. McKhann, of Ann Arbor, who will meet with the Camping Association group to advise on general medical matters which pertain to camping. The committee, as you know, has formulated, at the request of the secretary of the Academy, a definite program for the chairmen of the state camping committees. This report is again called to your attention. Considerable activity has taken place during the past year in various centers, both directly and indirectly through the influence of the national committee. I refer to work of our various state

chairmen, such as Dr. Snedeker, of Boston, who has been responsible for the publication of a Camping Number of the Massachusetts Department of Public Health publication, "The Commonwealth." (See attached copy.) Activities of a similar nature have gone on in other communities.

We have been in contact with Dr. Sharp, of Life Camps, Inc. He asked us to join his National Camp group and also offered us two scholarships last summer. We were unable to locate two younger men who were free to take advantage of this opportunity.

One of our committee has made a careful résumé of existing national legislation on summer camps for children. He has also formulated a tentative bill which we hope at some future date can be presented for state and national consideration.

As you may realize, the Committee on Camps receives numerous communications from various parts of the country for advice concerning medical supervision of camps.

There are two particular problems which confront the committee. In the first place, we have not as yet been able to work in an effective way with any existing camp organization. It was decided that our interest should be largely with the so-called organizational or nonprofit camps. These organizational camps work independently of the American Camping Association. For instance, in Boston there are ninety-two camps which only recently have been organized under a local camping committee. It is felt by the committee that we are distinctly an advisory group and must work through some existing agency. It is our hope and belief that the American Camping Association will eventually serve all the organizational camps and solicit our advice.

The second problem concerns a lack of interest, or better, of knowledge among physicians in regard to camps. We feel that this is an educational problem and that we cannot successfully act in the capacity of advisers unless we have had actual experience in camp work. It is our suggestion that through the state chairmen we can interest members of the Academy to take an active part, not only in regard to medical matters, but also in regard to general camping activities of their locality. It might thus be possible for Academy members to be chairmen of camp committees in their community.

Report of the American Board of Pediatrics:

The members of the American Board of Pediatrics appointed by the American Academy of Pediatrics submit the following report of the work of this Board from November 1, 1940, to October 1, 1941.

Three examinations have been held since our last report, as follows: Memphis, Nov. 16 and 17, 1940; New York City, March 30 and 31, 1941; and Chicago, May 18, 1941. One hundred and eighty-six applicants were examined at these meetings, of whom 82 per cent were passed and certified, while the remaining 18 per cent were either failed or conditioned. These percentages are practically the same as given last year. To date 1,717 certificates have been issued, one of which was revoked following our last annual meeting due to falsification of credentials. As we did last year, we are continuing to give both written and oral examinations. I might add that the results of the two examinations tally very closely.

As you know, we are holding a two-day examination at the time of the annual meeting of the Academy in Boston and it is planned to hold three oral examinations during the Spring of 1942: at Philadelphia at the time of the meeting of Region I, in Cleveland at the time of the meeting of Region III, and in Los Angeles at the time of the meeting of Region IV.

The Board of Pediatrics did not publish a Directory of Licentiates during the year, but we are cooperating with the Advisory Board for Medical Specialists, a new edition of which will be off the press in February, 1942.

At the last annual meeting of the Board of Pediatrics in Memphis on November 16, 1940, in line with the National Defense Program, it was decided to allow candidates for examination to substitute one (1) year of military service for one of the required two years of pediatric practice and/or continued study. This military service cannot be substituted for any of the required preliminary training, however.

To date the application fee has not been raised and no new members have been elected to this Board. However, Dr. Veeder's term of office is up this year and it will be necessary for the Academy to act upon this matter.

Respectfully submitted,

HAROLD C. STUART
BORDEN S. VEEDER
ALFRED A. WALKER

News and Notes

The attendance at the meeting of the Academy in Boston was as follows:

Official Guests	43
Associate Members	3
Exhibitors	62
Visitors	250
Members	540
Women	188
Total	1,086

After careful consideration, the *American Board of Pediatrics* at its annual meeting in October found it necessary to increase its fee from $30.00 to $50.00, effective May 1, 1942. The Board will accept all applications from eligible physicians postmarked prior to May 1, 1942, at the old rate of $30.00.

This action was taken with considerable regret and only after it had been demonstrated that the work of the Board could not continue without an increase in income. In its early years a large number of pediatricians were certified on record without examination, which resulted in a considerable sinking fund being built up. During the past two years this backlog has been seriously impaired, and this step is being taken to prevent running out of funds during the next few years when applications will be fewer and expenses no less. As it has been pointed out, the fee previously charged has been lower than that found necessary by the other certifying boards.

At the annual meeting Dr. Horton Casparis was elected president of the Board, succeeding Dr. Borden Veeder whose term expired this year.

Comments

The eleventh annual Academy meeting at Boston October 9 to 11 again demonstrated the steadily increasing importance of the Academy and the interest of pediatricians in their organization. There was a total registration of 1,086 of whom 540 were Academy members, a figure rarely reached in medical meetings. Despite the fact that the meeting was held at a point far distant from the central, western, and southern parts of the country, members were present from all of the states but three, and from four of the Canadian provinces. There are only five members in the three states not represented. There were forty-two exhibitors in the commercial exhibit and 31 in the scientific exhibit, a decided increase for both over previous years.

Four of the six sessions were given over to ten round tables (sixteen topics) and four panel discussions, going on simultaneously. On Thursday evening a general meeting was held on "The Role of the Pediatrician in National Defense" with Dr. Philip M. Stimson, Chairman of the Academy Committee on National Defense, Dr. Harold Stuart, Dr. Martha Eliot, of The Children's Bureau, and Dr. Thomas Parran, Surgeon General, U. S. Public Health Service as speakers. These addresses will be published in an early number of the JOURNAL.

At the general session on Friday the E. Mead Johnson Awards were presented, followed by the annual address of the President. (These papers appear in this issue.) The first award was given to Dr. Rene J. Dubos, of the Rockefeller Institute, and the second to Dr. Albert B. Sabin, of the Cincinnati Children's Hospital Research Foundation.

At the business meeting the usual officers' and committee reports were presented for discussion. Three of the recipients of South and Central America Pediatric Scholarships established by the Academy were introduced and gave greetings from their national pediatric societies. Dr. Edward C. Mitchell, the new president of the Academy, was unable to be present on account of illness and a telegram was sent him wishing a speedy recovery. Dr. Borden Veeder was elected Vice-President, and Dr. Lee F. Hill, of Des Moines, Chairman of Region III to fill the vacancy due to the death of Dr. A. Graeme Mitchell. Complete minutes will be found under the Academy Proceedings. Chicago was selected as the meeting place in 1942.

For the first time a clinic day was held on Wednesday, the day preceding the meeting. That it was welcomed and a success was shown by a large registration, although pediatricians of Boston and vicinity were requested not to register for the clinics. Between the morning and afternoon clinic sessions lunch was served at the hotel. The Thursday and Friday recesses, if they may be called that, were given over to committee luncheons. At the luncheon meeting for State Chairmen on Friday, thirty-six states and three provinces were represented. At this meeting a new Manual for State Chairmen, discussing the various activities of the Academy, how they are organized and how they function, was distributed. This manual prepared by Dr. Martmer should be of tremendous value to members assuming the responsibility of state chairman.

Everyone present was in agreement that they had never attended a more smoothly and efficiently run meeting. This was due to the tireless effort of Dr. Grulee and his office, the local committee headed by Dr. Lewis Webb Hill, and the hotel management. The local committee arranged a most interesting trip on Friday for the ladies to places of historical interest near Boston. The annual dinner on Friday night was followed by the pediatric drama, "The Disappearing Diapers," or "Gone With the Wind," and dancing. Over 800 members, guests, and wives attended. It was needed relaxation for a heavy steady program of meetings.

One unannounced item which drew much attention and comment was an exhibition of nearly seventy etchings and water colors by Dr. A. Graeme Mitchell, arranged for by Mead Johnson and Company. It was a "one man show" of which a professional artist might have been proud.